A dissertation on

AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLY DIAGNOSED DEPRESSIVE DISORDER PATIENTS

Submitted to the

THE TAMILNADU Dr.M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations for the award of the degree of

MASTER OF SURGERY BRANCH- III

(OPHTHALMOLOGY)

GOVERNMENT RAJAJI HOSPITAL

MADURAI MEDICAL COLLEGE

MADURAI

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

MAY 2019

CERTIFICATE

This is to certify that the dissertation titled **"AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLYDIAGNOSED DEPRESSIVE DISORDER PATIENTS "**submitted by **Dr.P.MENAKA** to the faculty of ophthalmology, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.S.Degree (Ophthalmology) is a bonafide research work carried out by her under our direct supervision and guidance.

Dr.K.KAVITHA MS,DNBOPHTHAL.,
Hod and Professor,
Department of Ophthalmology
Government Rajaji Hospital
Madurai Medical College
Madurai - 625020

Dr.D.MARUDHUPANDIAN,M.S, FICS
The **Dean**
Madurai Medical College Madurai

CERTIFICATE FROM GUIDE

This is to certify that the dissertation titled **"AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLY DIAGNOSED DEPRESSIVE DISORDER PATIENTS"** submitted by **Dr.P.MENAKA** to the faculty of ophthalmology, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.S.Degree (Ophthalmology) is a bonafide research work carried out by her under my direct supervision and guidance.

Dr.E.Rajeswari., M.S, ophthal
Assistant Professor,
Department of Ophthalmology
Government Rajaji Hospital
Madurai Medical College
Madurai - 625020

Dr.K.KAVITHA MS,DNB OPHTHAL,
Hod and Professor,
Department of Ophthalmology
Government Rajaji Hospital
Madurai Medical College
Madurai - 625020

DECLARATION

I,**Dr.P.MENAKA**solemnly declare that the dissertation titled **"AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLY DIAGNOSED DEPRESSIVE DISORDER PATIENTS"**has been prepared by me.This is submitted to **The Tamil Nadu Dr.MGR Medical University, Chennai** in partial fulfillment of the rules and regulations for the M.S.Degree Examination in Ophthalmology to be held in May 2019.

Dr.P.MENAKA

PLACE: Madurai Medical College, Madurai – 625020.

DATE:

ACKNOWLEDGEMENT

I express my sincere thanks and gratitude to **Prof.Dr.D.MARUTHUPANDIAN MS.,FICS.,** the dean, GRH and MMC Madurai for permitting me to conduct this study. I express my gratitude to **Prof.Dr. KAVITHA MS., DNB.,** Professor and Head of the department of Ophthalmology,Government Rajaji Hospital and Madurai Medical College,Madurai,for his expert guidance and advice in permitting me to conduct and complete this study.

I also owe my sincere thanks to **DR.N.PARVATHASUNDARI MS,DO**Associate Professor ,department of Ophthalmology,Government Rajaji Hospital,for her support and encouragement to me in performing this study.

I am grateful to my beloved co-guide **Dr.E.RAJESWARI MS.,**AssistantProfessor, department of Ophthalmology,Government Rajaji Hospitalfor her valuable guidance and encouragement throughout this study period.

I thank all my **ASSISTANT PROFESSORS** of my department for their support and encouragement in conducting this study.

I express my deep sense of gratitude to **Dr.T.KUMANAN MD,DPM HOD** and **PROFESSOR of PSYCHIATRY** for evaluation of their patients and their support to this study.

I am grateful to the staff of department of Ophthalmology and my fellow post graduate colleagues for their valuable help throughout this study. Last, but not the least, my profound gratitude to all the ‘patients’, to whom I owe everything because, this venture would not have been possible without them.

PART I

CONTENT

INTRODUCTION

Dry Eye Disease (DED) is a common multifactorial problem with varying prevalence rate of 5-34%.. Numerous exposures—including medication use, hormonal changes, environmental exposures, and neural alterations—are involved in the pathogenesis of dry eye. Common symptoms of dry eye patients include pain, irritation, itching, burning, and grittiness.

Dry eye results in discomfort, visual disturbances and tear film instability with potential damage to ocular epithelial surface which is accompanied by increase in tear osmolarity and inflammation.

Dry eye syndrome involves multiple risk factors that when disregarded can result in treatment failure and frustration both for the patients and the physician. Dry eye may lead to increase risk of infections, medications toxicity, contact lens intolerance, progressive ocular surface disease, scarring, cornea morbidity (keratinisation, corneal thinning, vascularisation), microbial and sterile corneal ulcer leading to perforation and finally severe visual loss. Hence correct diagnosis and appropriate management of dry eye is essential.

It poses a huge economic burden to patients if not evaluated for risk factors that may result in delay in treatment. It affects the quality of life of patients with

regards to daily visual acuity. It results in social stigma as a patient may have chronic red eye. Patient may go in for depression .

Like Dry eye disease,Depression also a chronic problem nowadays. Both will affect the quality of life.Many studies have been reported that an association between dry eye and depression, post-traumatic stress disorder and anxiety and dry eye.The prevalence of DED in depression is 29%.

EPIDEMIOLOGY

The prevalence of dry eye has not been determined accuratelydue to the lack of a single definition of the condition as well as the variability of criteria included in several studies. Howeverprevalence of dry eye disease to be between 5-34percent. The Beaver Dam Study demonstrated an incidenceof dry eye of 13.3 percent that significantly correlated withpatient age. Dry eye was apparently higher in women (14.7%)than men (11.7%).

TEAR FILM-ANATOMY

The precorneal tear film is the sheet of tears which covers the exposed interpalpebral portion of the globe and cornea. That portion overlying the cornea is the precorneal tear film.

For maintaining a moist surface over the cornea and for spreading of the tears blinking action of the eyelids is essential.

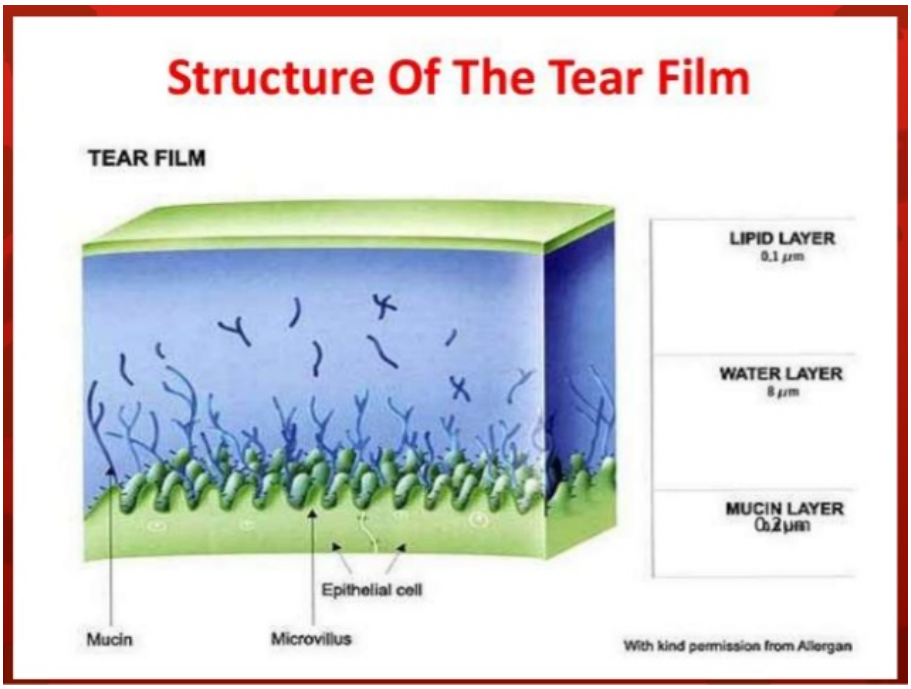
In 1928 Fischer first demonstrated the presence of precorneal layer.He used the principle of Reflectography(reflection of light on a photographic plate from the corneal surface.

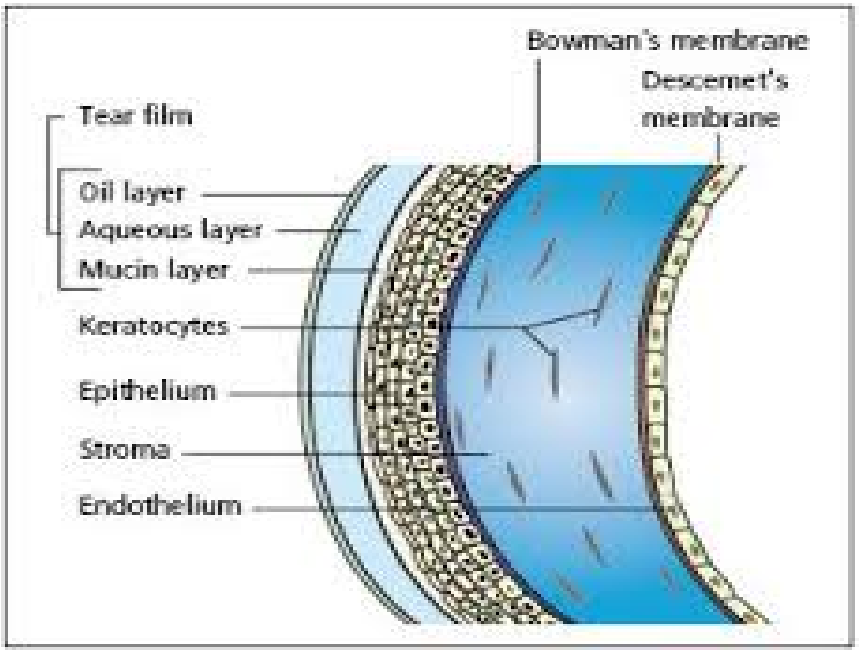
In 1950 wolff first described The original model of the tear film .it is a trilaminar structure consisting of an an outer lipid layer, an intermediate aqueous layer, inner mucus layer .

The tear film consists of 3 layers:

1. Lipid layer
2. Aqueous layer
3. Mucin layer

4.


Structure Of The Tear Film
TEAR FILM
LIPID LAYER
0.1 μm
WATER LAYER
8 μm
MUCIN LAYER
0.2μm
Epithelial cell
Mucin
Microvillus
With kind permission from Allergan

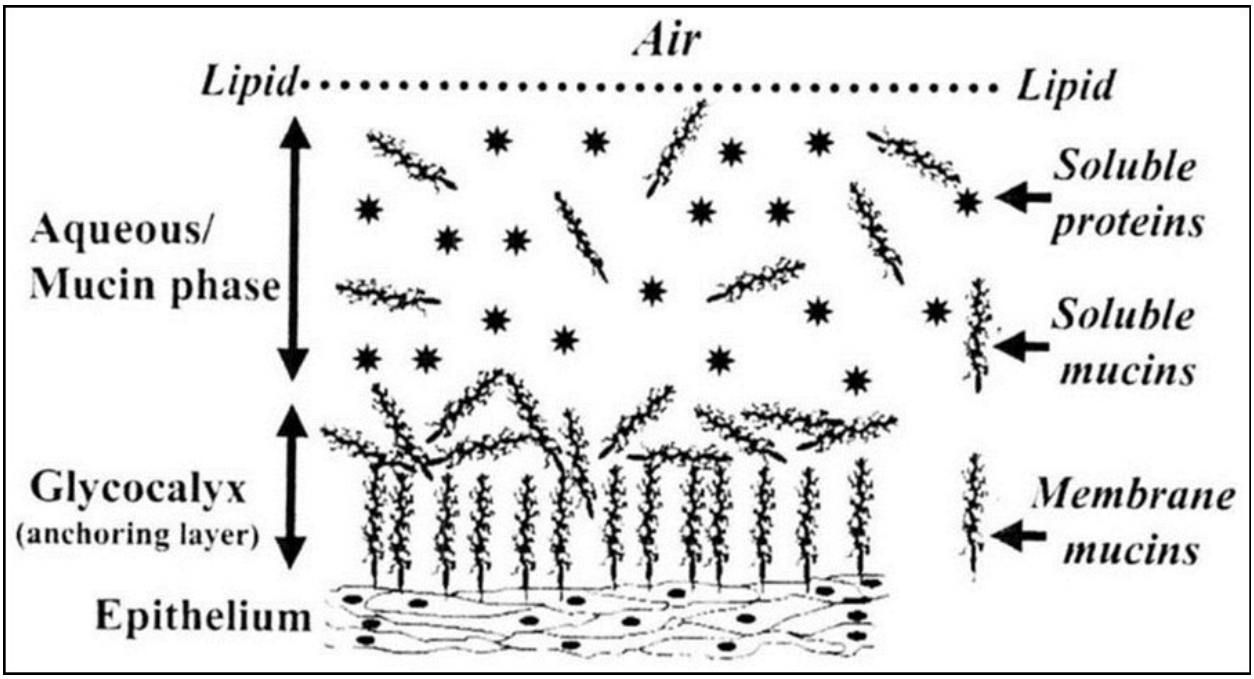

Bowman's membrane
Descemet's membrane
Tear film
Oil layer
Aqueous layer
Mucin layer
Keratocytes
Epithelium
Stroma
Endothelium

1.lipid layer-It is outer most layer.0.1 microns thickness.it is secreted by meibomian glands,zeiss and moll glands.

2.Aqueous layer-middle layer.main bulk of thickness of tear film is constituted by this layer.10 microns thickness.it is secreted by lacrimal gland and accessory lacrimal glands of Krause and wolfring.

3.Mucin layer-inner layer.thickness of 0.2-1 microns.secreted by conjunctivalgoblet cells,glands of manz,crypts of henle.

New model of tear film-Two layer structure , which consists of aqueous/mucus phase and an outer lipid layer is gaining acceptance in the dry eye community . Aqueous layer has dissolved mucins located in it;In lipid layer they are decreasing gradually . The tear film contains lot of proteins and salts .Major tear proteins are lactoferrin, lipocalin,and Lysozyme while carbonate, potassium, chloride, phosphate bicarbonate, sodium, calcium and ions are present . literature says that tear film contains proteomic biomarkers and they are useful in the diagnosis of ocular surface diseases like dry eye .



The Tear Film Aqueous/Mucus Phase

Mucins are high molecular weight glycosylated glycoproteins present in this layer of the tear film. Mucins are secreted by conjunctival goblet cells , while lacrimal gland, corneal and conjunctival surface epithelial cells secrets smaller amounts of mucin. tear breakup timeis influenced by Ocular mucins and play important roles in stabilization spreading and of tear film. In the apical surface of corneal and conjunctival epithelial cells Transmembrane mucins are anchored and the formation of the glycocalyx is facilitated. The glycocalyx is a combination of finger-like (microvilli) and ridge-like (microplicae) projections located on the apical surface of corneal epithelial cells which contains transmembrane mucins

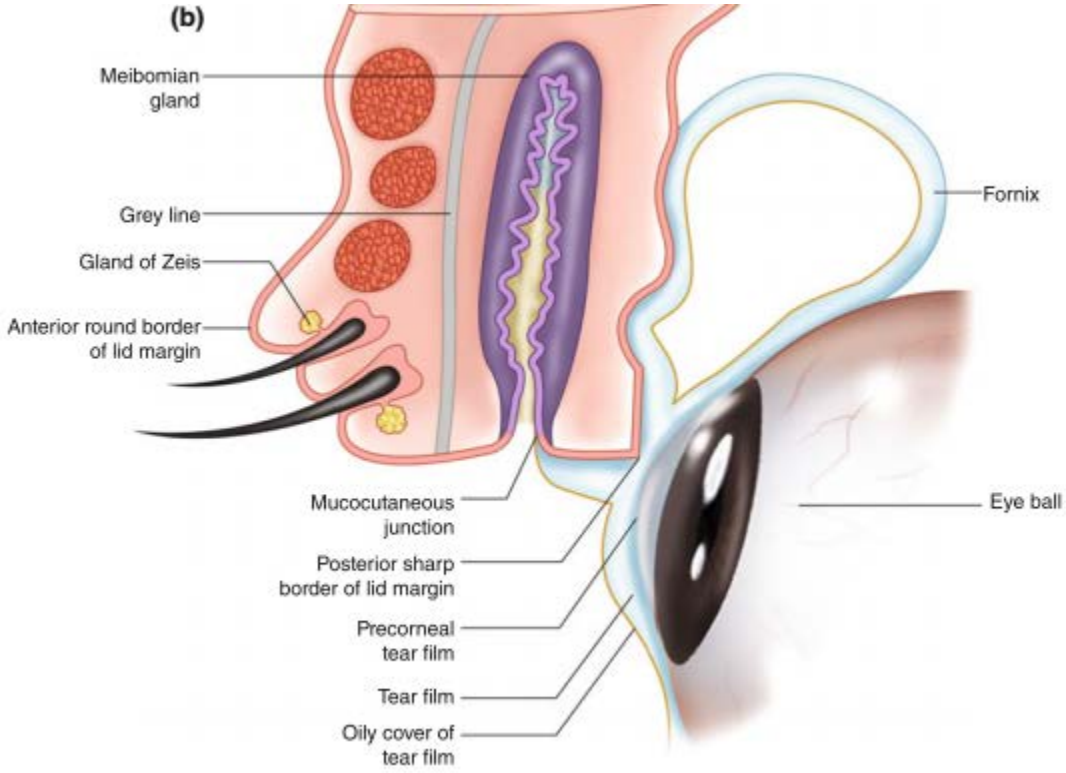
The glycocalyx is important because as it plays crucial role in stabilizing and spreading the tear film over the ocular surface. A another type of mucins, the secretory mucins, helps in holding fluids over the epithelial surface

The aqueous layer contributes the major portion of the tear thickness , the watery phase of the tear film. The aqueous is secreted primarily by the main lacrimal gland which is situated in a shallow depression of the frontal bone near the supero temporal portion of the orbit.

The lacrimal gland is a tubulo-acinar structure which has ducts. they open into the superior conjunctival fornix. Glands of Krause and Wolfring are accessory lacrimal glands.They also secretes aqueous but only little amount. The aqueous contains major component of water that is 98% , but also contains mucins, electrolytes, proteins, immunoglobulins, growth factors, , hormones, and inflammatory cells, desquamated epithelial cells, and metabolic waste. Electrolytes are important for maintaining tear pH around 7.5 , the integrity of the epithelium, and osmolarity . Tear film also contains Cytokines and chemokines . During epithelial cell stimulation ,there is increased secretions of these mediators into the tear film , but basal secretion occurs as usual.

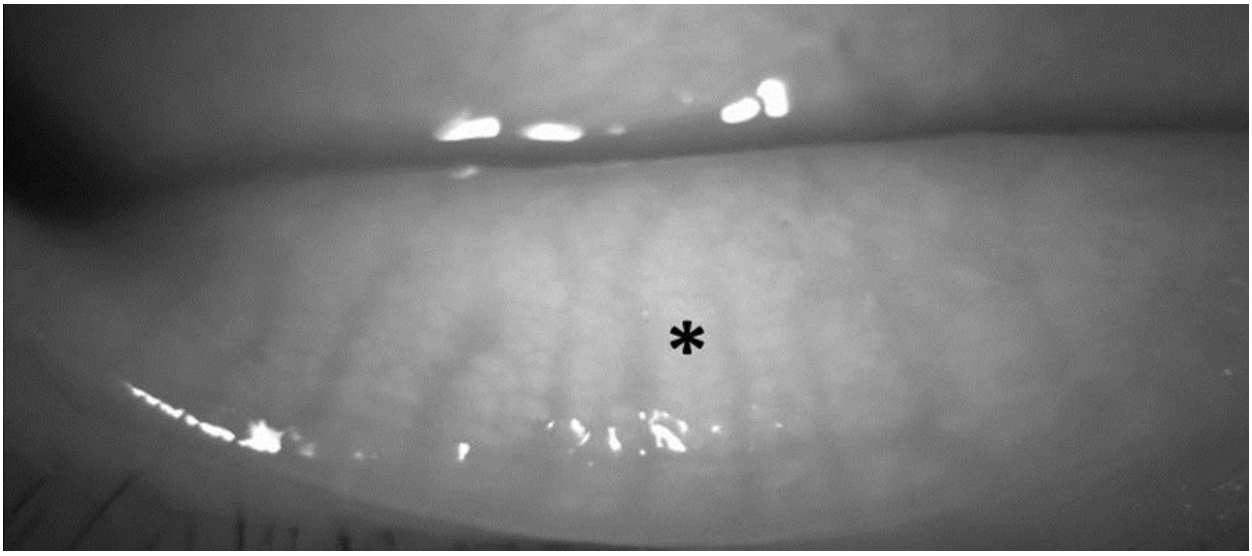
2.The Lipid Layer

The superficial and outermost layer of the tear film is formed by lipid layer. This layer is secreted primarily by the meibomian glands .Meibomian glands are situated within the tarsal plates of the both eyelids . The glands of Zeis and moll secretes a small amount of tear film lipid.



The meibomian glands are modified sweat glands and of holocrine type. upper lid contains 25-40 glands and lower lid contains 20-30. surrounding a main duct there are lot of secretory acini clusters in the single gland . small ductile connects these Clusters of acini to the main duct .In meibography Healthy meibomian glands appears as a “chain of onions” or“grapes-on-a-vine”

appearance .The main duct opens into the eyelid margin just anterior to the muco-cutaneous junction. The glands are arranged in a single row vertically parallel to each other .



Meibomian glands. The meibomian glands located within the lower eyelid are imaged by meibography (one gland marked with an asterisk). Note the grapes-on-the vine structure of each gland. The grapes are the individual acini that contain meibum-producing meibocytes while the vine is the duct that transfers meibum to the eyelid surface where it is deposited onto the tear film.

Secrections from meibomian glands are oily in nature.They are secreted by meibocytes.meibocytes are special type of cells which are located in the secretory

acini and produce the sebum that will finally be expressed from the gland . During the process of maturation , lipid production cell organelles increase in number and size .

The lipid droplets formed within the meibocytes are contained within a specialized membrane.It is derived from the smooth-endoplasmic reticulum . After full maturation of meibocytes,breaking of cell membrane occurs and its contents are released, into the ductal system includes proteins and nucleic acids,; the contents are now called as meibum . meibum is not expressed onto the lid margin immediately because the main duct of the gland is so long. Due to compression of tarsal plate by the orbicularis muscle and gradual increase of meibum that is constantly being released from other meibocytes meibum is pushed toward the gland opening .

The meibum is finally delivered to the ocular surface with the help of Riolan's muscle; this muscle surrounds the duct near its opening at the eyelid margin. During each blink this Riolan muscle contracts and forcing the meibum out from the main duct onto the lid margin surface during closure . during the blink's upstroke The meibum is then spread onto the tear film lipid layer. Upward motion of the upper eye lid is followed by The movement of the lipid layer, but generally it lags the upstroke by approximately 1-2 seconds and in dry eye patients it is prolonged .

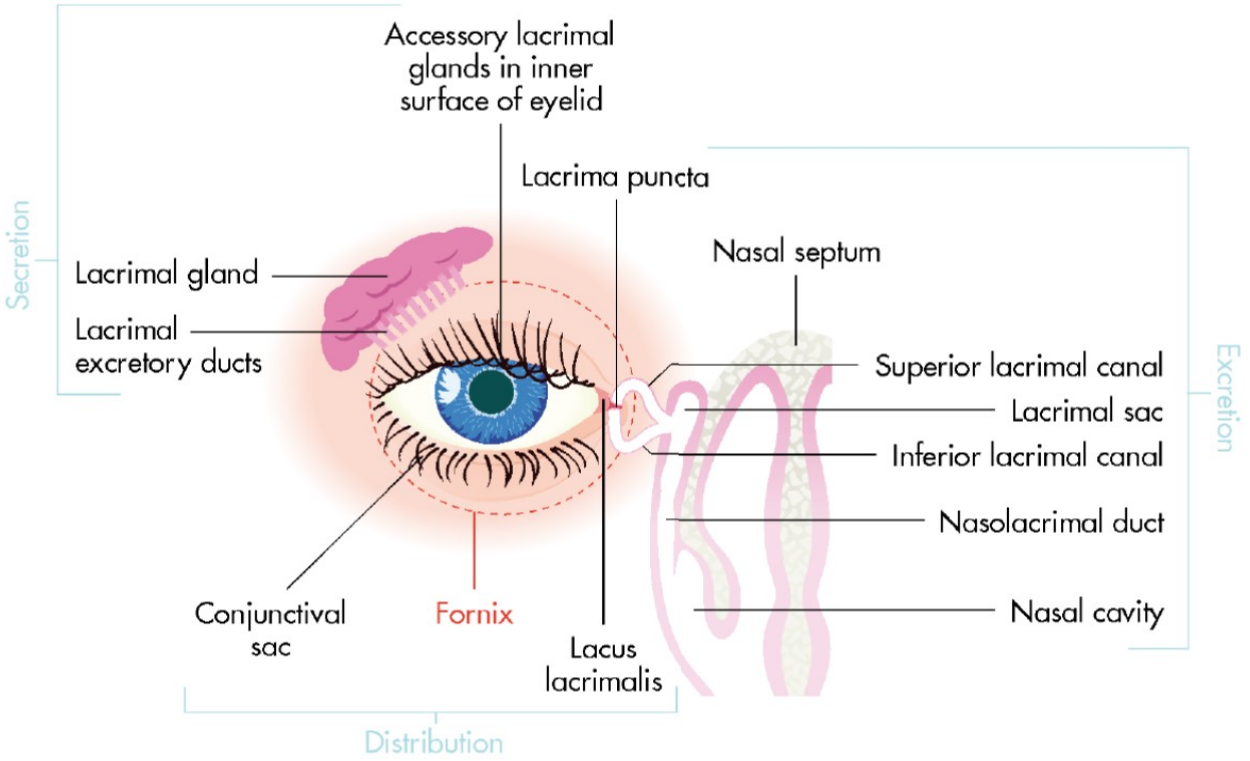
The tear film lipid layer is comprised of both meibum ,attached and intercalcated proteins.it consists of two layers.The inner layer lies just anterior to the aqueous layer which is called polar layer.it contains polar lipids.outer layer is non polar lipid layer and it is exposed to air.inner lipid layer acts as an interface between the nonpolar layer and aqueous layer by immersing their hydrophobic tails into the nonpolar layer and their hydrophilic heads into the aqueous layer.

lipocalin one of the tear protein increases stability and spreading of the lipid layer by decreasing surface tension within the aqueous by forming complexes with the polar lipids .

Lipid components in the polar sublayer include phospholipids, sphingomyelin, ceramides, cerebrosides, and very long chain (*O*-acyl)-*O*-hydroxy fatty acids . Nonpolar components include hydrocarbons, very long chain acyl-ceramide, wax and cholesterol esters, triacyl glycerols, and free fatty acids . In dry eye states, low levels of phospholipids, sphingomyelins, and alcohols of wax and cholesterol esters have been reported.In dry eye fatty acid composition is changed . Imaging with interferometry has shown delays in lipid spreading and increased thinning in dry eye individuals.

The total volume of the tear film is 7-9 µL basal (non-reflex) tear secretion rate is 1-2 µL/minute ., thickness of Tear film is estimated By using varying techniques.it is ranging from 7-40 µm . Tear film thickness measurements are important as they provide information on tear volume and evaporation rates when the eyes are open ,

The Ocular Surface Structures



The conjunctiva is a thin, translucent mucous membrane .It covers the inner side of the eyelids .It extends from the muco-cutaneous junction to the limbus and contains approximately 2-10 layers of nonkeratinized stratified or columnar epithelium and is highly vascularized. specialized epithelial cells are present on the

conjunctival surface called goblet cells.They secrete numerous mucins and supply the majority of the mucin to the tear film. The conjunctival epithelium secretes inflammatory cytokines which are involved in the pathogenesis of dry eye

At limbus, the conjunctiva transitions into the cornea, a transparent, avascular structure. There are five layers in the corneal epithelium. Type of epithelium is nonkeratinized stratified squamous epithelium and is one-tenth of the total corneal thickness.

.**FUNCTIONS OF TEAR FILM**

1)It acts as a lubricant for the lids and preocular surface.It reduces the frictional forces which are developed during blinking movements and rotational movements of the eye ball.

2)It washes away the debris and noxious irritants.

3)It transfers oxygen from the ambient air to the cornea.

4)corneal epithelial cells are very sensitive.They could not survive in dry surface.Tear film keeps the corneal and conjunctival surface moist.

5)Tear film has antibacterial substances like lactoferrin,lysozyme,betalysin,immunoglobulins and other proteins.so that it

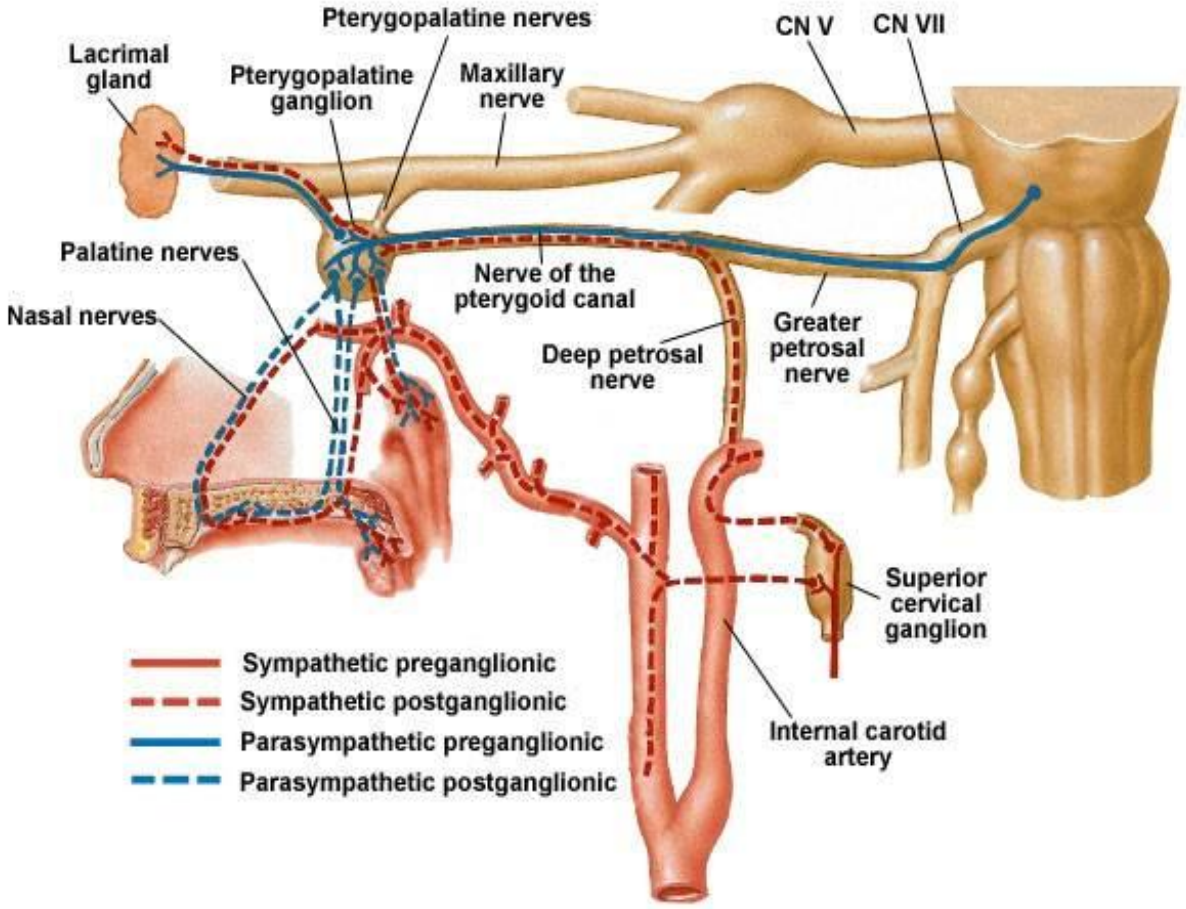
prevents infections.

6)In any injury it gives the pathway for white blood cells.

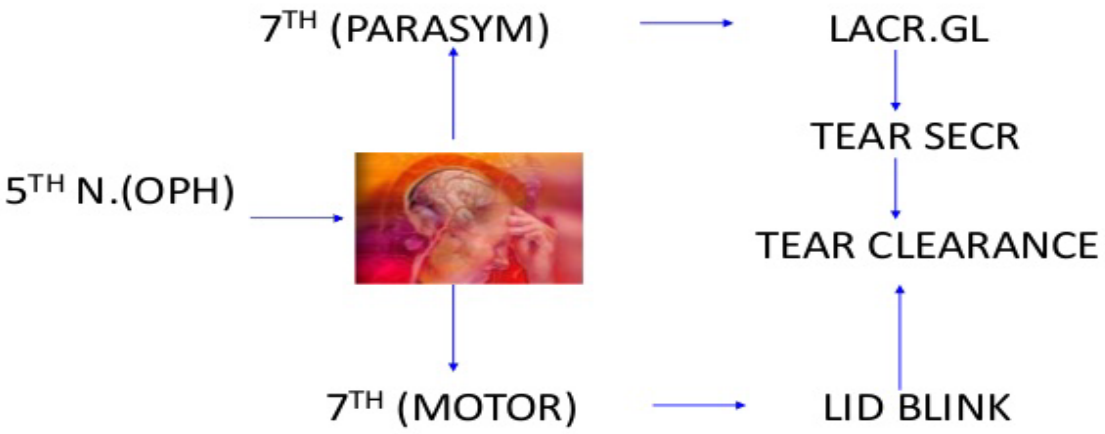
7)It forms smooth optical surface on the cornea by filling in and smoothening out small surface irregularities in the corneal epithelium.

Regulation of Tear Production

The lacrimal gland innervation is complex. The reflex arc is, particularly important, involving fibres from the 5^{th} cranial nerve in the cornea, conjunctiva and surrounding tissues. There is also innervation by both the parasympathetic and the sympathetic systems, inducing positive and negative control of secretion respectively. The parasympathetic route ,starting from the lacrimatory nucleus in the brainstem of the facial nerve (cranial nerve VII), parasympathetic fibres follow the greater superficial petrosal nerve to the pterygopalatine ganglion; the conventional view is that from there the secretory fibres of the lacrimal nerve follow the zygomatico-temporal nerve and join the lacrimal nerve of the ophthalmic division of fifth cranial nerve and enter the lacrimal gland. However, there is evidence that a number of rami orbitales pass from the pterygopalatine ganglion and some of these travel directly to the lacrimal gland .



NEURONAL REFLEX ARCS



DRY EYE DISEASE

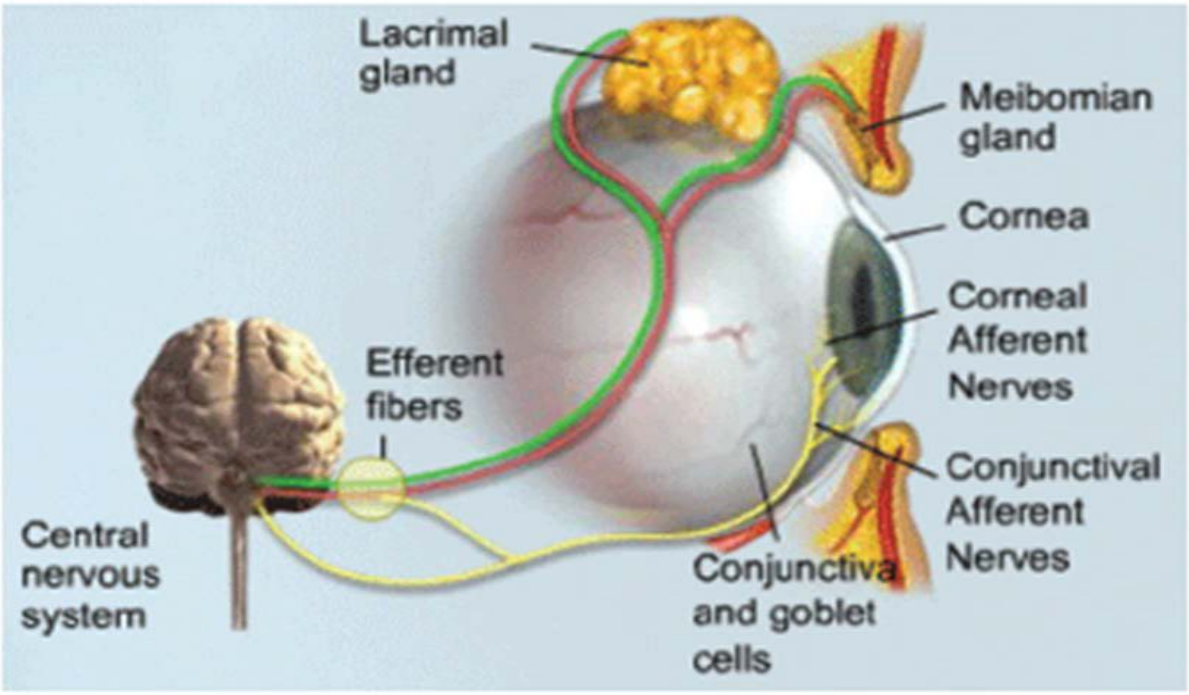
Dry eye isa common condition that is often under diagnosed. Normal vision requires moist healthy ocular surface. A sufficient quality of tears, normal composition of tears film (which comprises of lipid, aqueous, mucin layer), lid closure is require to maintain healthy ocular surface.

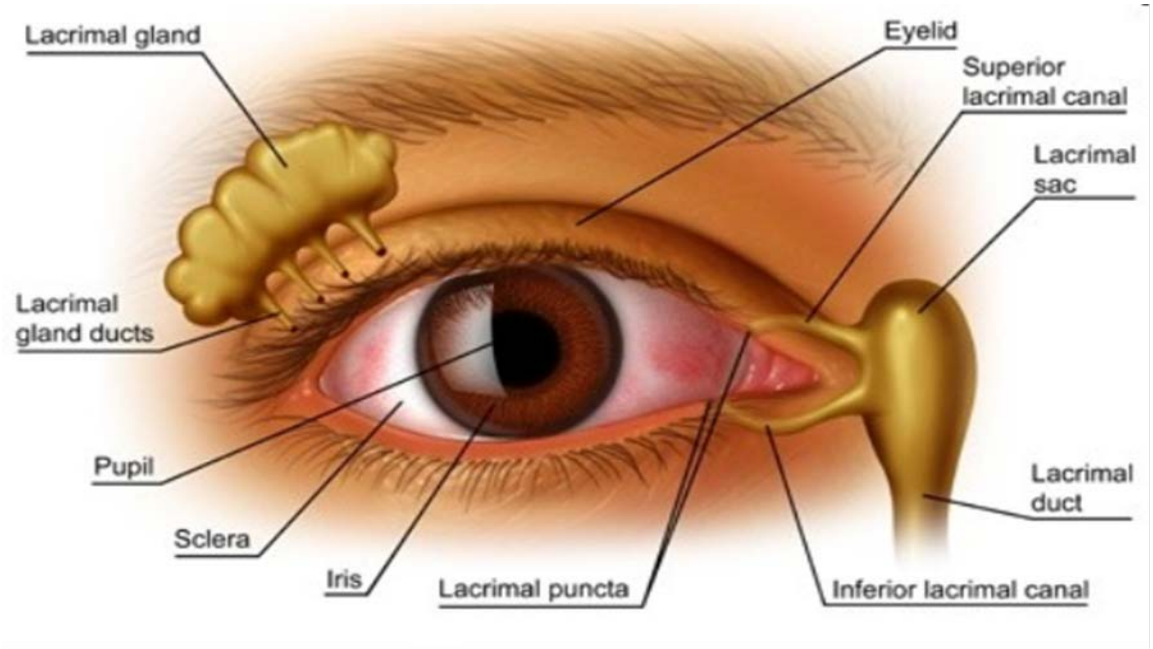
Dry eye is a disorder characterised by either quantitative decrease or qualitative change in precorneal film resulting in spectrum of pathological changes that may adversely affect the ocular surface resulting in ocular surface disorders often leading to conjunctival squamous metaplasia and puncta epithelial erosion of cornea.

The International Dry Eye Workshop (2007) defined dry eye as a multifactorial disease, of the tears and ocular surface that results in symptoms of discomfort,, visual disturbance, and tear film instability with potential damage to the ocular surface. .It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

Dry Eye Disease is a disorder of **lacrimal functional unit.** It is not a single disease entity. The lacrimal functional unit consists of lacrimal glands,meibomian glands ,ocular nerves,goblet cells,ocular surface including cornea, conjunctiva, eyelids.

Figure 1. Lacrimal Functional Unit





Factors in the Pathogenesis of Dry Eye Disease

• Genetic predisposition

• Hormonal insufficiency:

– Age related

– Menopause

– Androgen insufficiency

• Systemic autoimmune disorder

- Insufficiency of spread of tears

• Age related atrophy of lacrimal gland

• hepatitis C, human immunodeficiency virus, Epstein-Barr,cytomegalovirus

• Neurotrophic keratitis

• Video display terminal

• Environmental stress.

• Iatrogenic

– LASIK

– Contact lens

– Medications—systemic/topical

Causes for Ocular Surface Damage in Dry Eye Disease

Although , the tear film has been described as three layered structure, new concept of the tear-ocular surface structure being that of a metastable tear film.It consists of an aqueous gel with a gradient of mucin content decreasing from the ocular surface to the undersurface of the outermost lipid layer. changes in any one of the layer leads to breakdown in the other, leading to a vicious cycle of damage. The causes for ocular surface damage are:

1. **Unstable tear film (due to):**

– Mucin deficiency (cicatricial conjunctival disorders).

mucin layer loss -----the shearing off of the epithelial cells -----ocular surface irritation and inflammation .

– meibomian gland dysfunction-leads to lipid deficiency due to Evaporative loss .

– inadequate spreading of tears due to Mechanical cause.

2.Hyperosmolarity of tears*:*

Chronic hyperosmolar state leads to evaporative damage of the ocular surface.Due to osmotic mechanism and by inflammatory activity Hyperosmolar tears act as toxic agents to the conjunctival and corneal epithelia.

3. Blink-related microtrauma*:*

In the presence of lubrication deficiency,The shearing effect caused by the movement of the upper lid over the cornea causes exfoliation of corneal epithelial

cells with exposure of the deeper layer of cells which do not have microvilli leading to tear film instability.

4. Loss of corneal sensation*:*

In the normal state, subthreshold sensory input from the cornea and conjunctiva alters the lacrimal and meibomian glands secretory activity via the efferent sympathetic and parasympathetic innervation. The individual is usually not aware of the sensation from the environment.

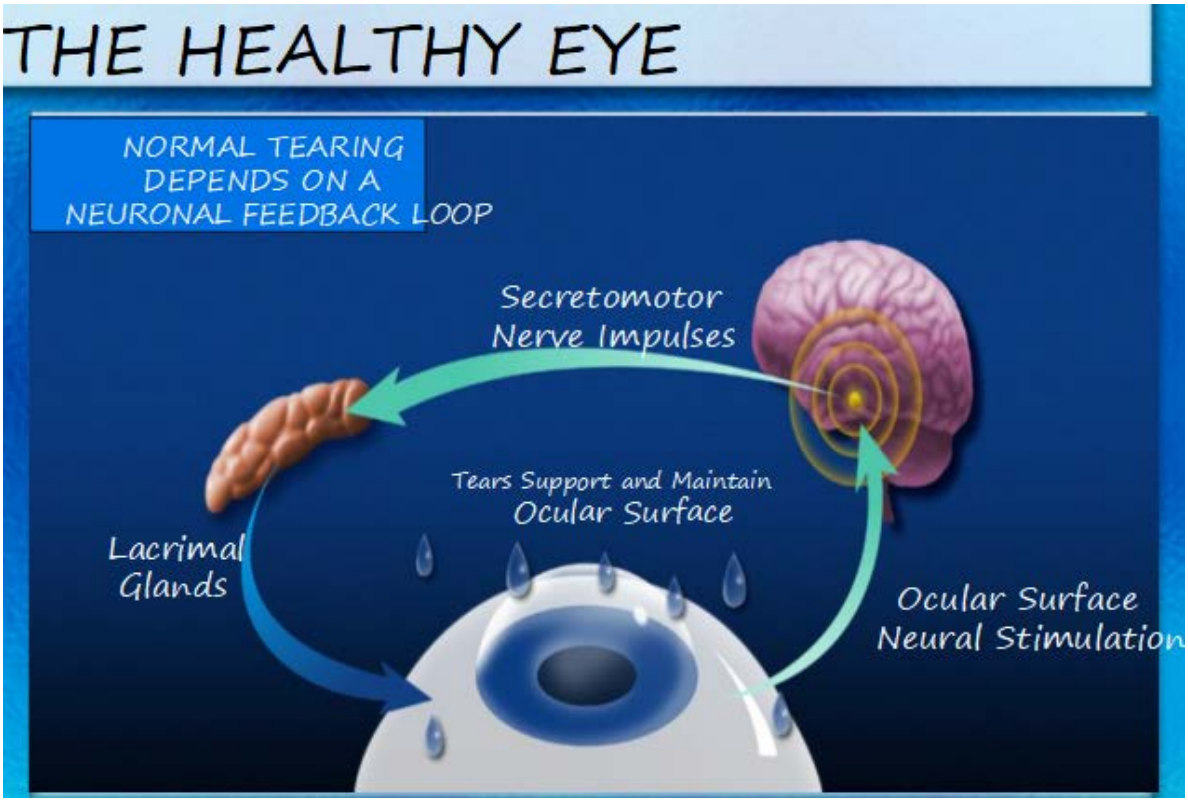
In contrast A suprathreshold sensation makes the individual more aware of the stimuli and causing severe pain.

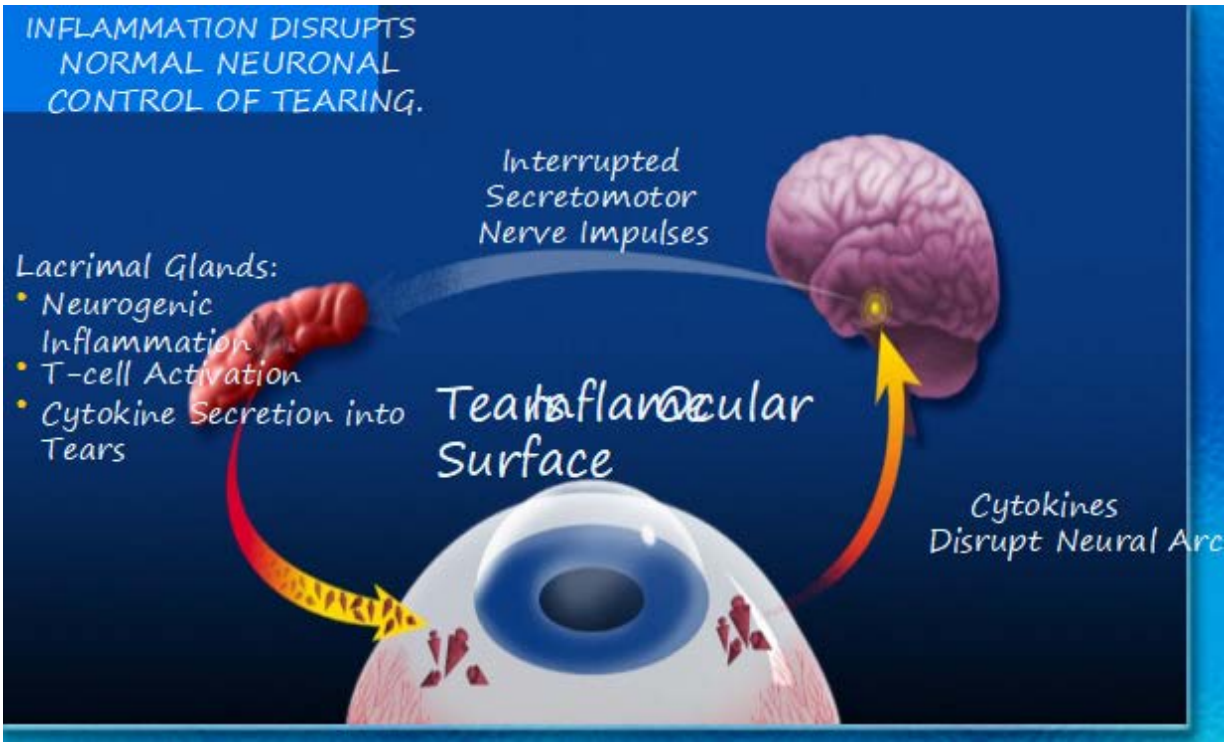
This is due to a number of involuntary reflexes being activated are reflex lacrimation, the blink reflex, a cardiovascular reflex and the Bell's phenomenon.These reflexes are nonsuppressible and protecting the eye from the potential danger.

In punctate corneal epitheliopathy, The sensation will be higher due to tear film breakdown is due to the disruption of the tight junctions in the apical cell layer of the epithelium that allows greater access of the environmental stimuli to the sensory nerve endings. , the intact neural loop, gets disrupted under stressful conditions.

5. Inflammation:

Inflammation ultimately forms the most importanteither primary as a part of the underlying disorder or secondary to all above mentioned factors, .





CLASSIFICATION OF DRY EYE

The International Dry Eye Workshop (DEWS) recently developed a 3-part classification of dry eye, based on

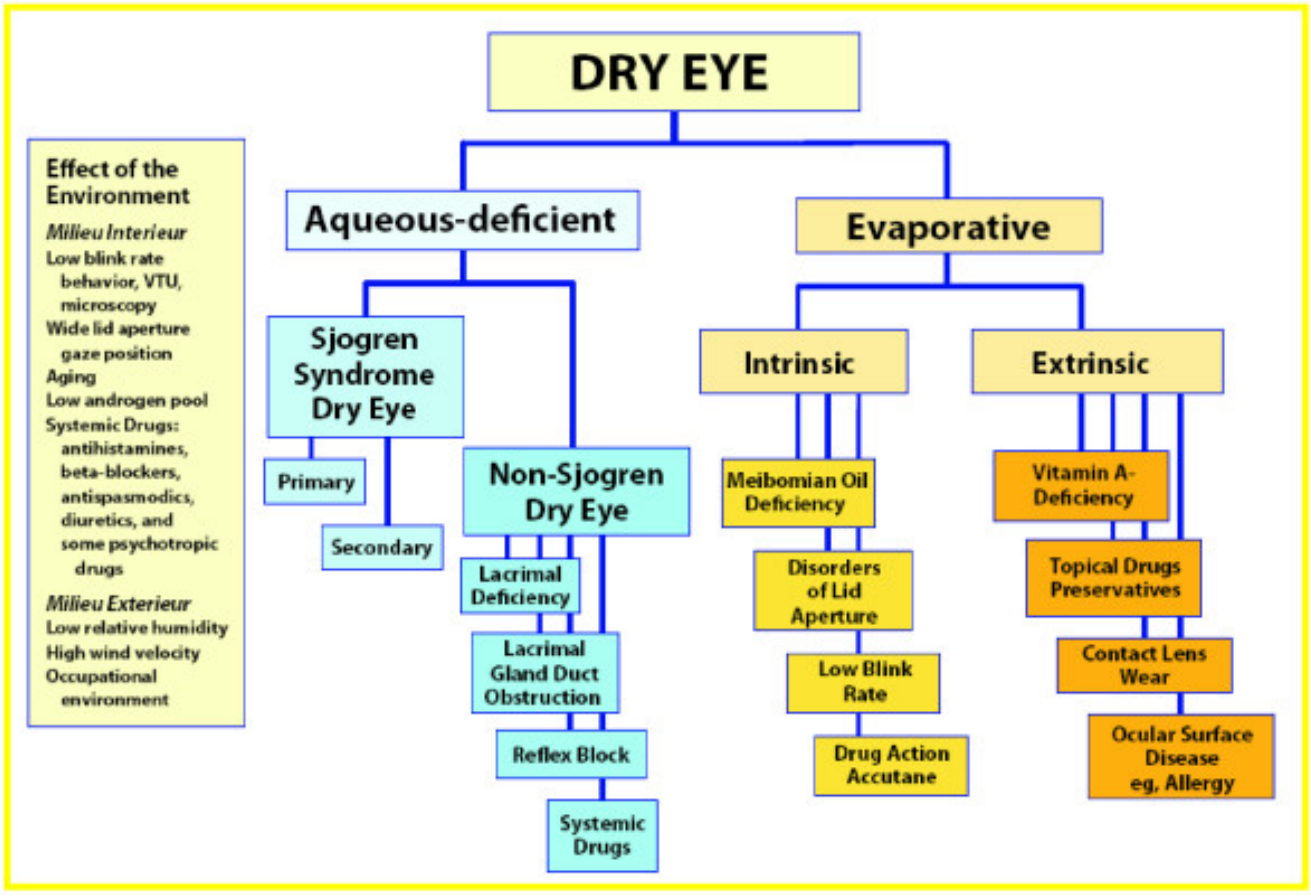
1)etiology,

2) mechanisms

3) disease stage.

ETIOLOGICAL CLASSIFICATION

AQUEOUS DEFICIENCY **EVAPORATIVE TYPE**



Aqueous deficiencycan be further classified as follows:

Non-Sjögren syndrome-main lacrimal gland deficiencies

- Idiopathic
- _Familial dysautonomia
- Age-related dry eye
- Congenital alacrima (e.g. Riley-Day syndrome)
    - Secondary lacrimal gland deficiencies
- Lacrimal gland infiltration
- Lymphoma

- Graft vs host disease
- Amyloidosis
- Sarcoidosis
- HIV diffuse infiltrative lymphadenopathy syndrome
- Trachoma
- AIDS
- Hemochromatosis
- Systemic vitamin A deficiency (xerophthalmia)—Malnutrition, intestinal malabsorption from inflammatory bowel disease, fat-free diets, bowel resection or
- chronic alcoholism
- Lacrimal gland denervation
- Lacrimal gland infectious diseases
- Lacrimal gland ablation
- Lacrimal obstructive disease
- _ Erythema multiforme and Stevens-Johnson syndrome
- Chemical and thermal burns
- Trachoma
- Endocrine imbalance
- Postradiation fibrosis.

- Ocular cicatricial pemphigoid

Medications—Antihistamines, anticholinergics, , antiparkinsonian agents, beta-blockers, phenothiazines,atropine, oral contraceptives, anxiolytics, diuretics, antiarrhythmics, topical preservatives in eye drops, topical anesthetics, and isotretinoin.

• Reflex hyposecretion—Reflex sensory block and reflex motor block

- Neurotrophic keratitis—Fifth nerve/ganglion section/injection/compression
- Infective—Herpes simplex keratitis, herpes zoster ophthalmicus
- Topical agents—Topical anesthesia
- Systemic medications—Beta blockers, atropine-like drugs
- Corneal surgery—Limbal incision (e.g. extracapsular cataract extraction), keratoplasty, refractive surgeries
- Chronic contact lens wear
- Diabetes
- Aging
- Cranial nerve VII (CN VII) damage Multiple neuromatosis

Sjögren syndrome

• Primary [no associated connective tissue disease (CTD)]

• Secondary (associated CTD)

- Rheumatoid arthritis

- Systemic lupus erythematosus
- Progressive systemic sclerosis (scleredema)
- Primary biliary cirrhosis
- Interstitial nephritis
- Polymyositis and dermatomyositis
- Polyarteritis nodosa
- Hashimoto thyroiditis
- Lymphocytic interstitial pneumonitis
- Idiopathic thrombocytopenic purpura
- Hypergammaglobulinemia
- Waldenstrom macroglobulinemia
- Wegener granulomatosis.

Evaporative losscan be further classified as follows:

Intrinsic causes

- Meibomian gland disease
    - Reduced number—Congenital deficiency, acquired meibomian gland dysfunction
    - Replacement—Distichiasis, distichiasis lymphedema syndrome, metaplasia
    - Meibomian gland dysfunction

- Hypersecretory—Meibomian seborrhea
- Hyposecretory—Retinoid therapy

– Obstructive—anterior blepharitis, systemic disease (e.g.acne rosacea, seborrheic dermatitis, atopy, ichthyosis,psoriasis), syndromes (e.g. anhidrotic ectodermal dysplasia, ectrodactyly syndrome, Turner syndrome),and systemic toxicity (e.g. 13-cis retinoic acid.

cicatricial, primary or secondary to local disease (e.g. chemical burns,trachoma, pemphigoid, erythema multiforme, acne rosacea)

• **Low blink rate**

– Physiological phenomenon, such as during performance of tasks that require concentration (e.g. working at a computer or a microscope)

– Extrapyramidal disorder, such as Parkinson disease (decreasing dopaminergic neuron pool).

• **Disorders of eyelid aperture and eyelid/globe congruity**

- Exposure (e.g. craniostenosis, proptosis, exophthalmos, high myopia)

- Lid palsy
- Ectropion
- Lid coloboma.

• **Drug action** (e.g. Accutane)

Extrinsic causes

• Vitamin A deficiency

– Development disorder of goblet cells

– Lacrimal acinar damage.

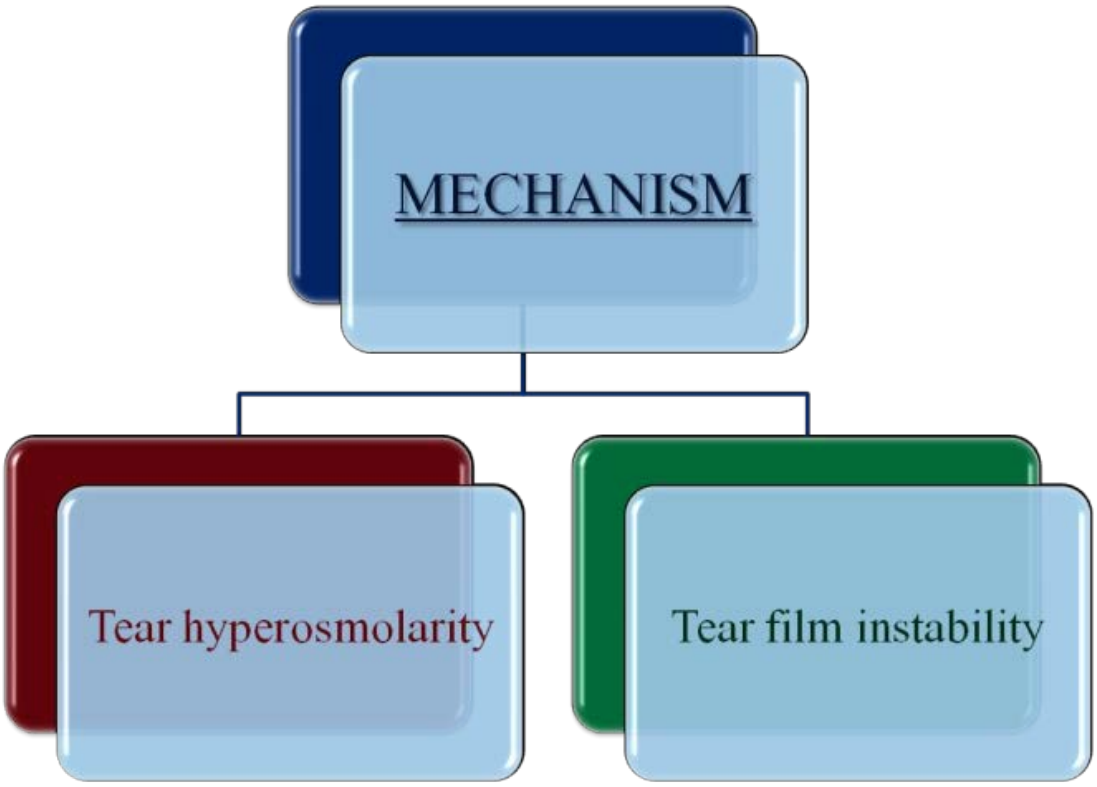
• Topical drugs and preservatives (surface epithelial cell damage)

• Contact lens wear

• Ocular surface disease (e.g. allergy).

MECHANICAL CLASSIFICATION

- **Tear film hyperosmolarity**
- **Tearfilm instability**



Classification of dry eye on the basis of severity

Delphi Panel Report classify the dry eye on the basis of severity and it is third component of DEWS

DEWS Dry Eye Severity Grading Scheme

Dry Eye Severity Level	1	2	3	4*
Discomfort, severity and frequency	Mild and/or episodic occurs under environ stress	Moderate episodic or chronic stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity limiting episodic	Annoying, chronic and/or limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/-	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked/central	Severe punctate erosions
Corneal/tear signs	None to mild	Mild debris, ↓ meniscus	Filamentary keratitis, mucus clumping, ↑ tear debris	Filamentary keratitis, mucus clumping, ↑ tear debris, ulceration
Lid/meibomian glands	Meibomian gland dysfunction (MGD) variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
Fluorescein tear break-up time	Variable	≤ 10 seconds	≤ 5 seconds	Immediate
Schirmer score	Variable	≤ 10 mm/5 min	≤ 5 mm/5 min	≤ 2 mm/5 min

*Must have signs and symptoms.

Source: *The Ocular Surface*, April 2007, Vol. 5, No. 2

DIAGNOSTIC TESTS

The tear film integrity and the ocular surface are very much important in maintaining optical clarity of the cornea.

Dry eye diseases could affect the clarity of cornea thus results in breakdown of ocular surface and visual impairment .

Currently, there are no single criteria for dry eye diagnosis,multiple diagnostic tests are used to assess the condition .This is the main disadvantage of this disease .so only it has varying prevalence rate.This needs a detailed history taking and examination. A number of questionnaires are available for dry eye symptomatology evaluation , including severity, quality of life, effect on daily activities .

HISTORY TAKING

History taking is ignored most of the times in an ophthalmic evaluation due to the the ability of the slit-lamp biomicroscope to detect the cause of the patient's problem.but still, history taking forms a vital part of the ocular examination .It reveals associated conditions which could aggravate the ocular problem.

- Women particularly postmenopausal women are most commonly affected by dry eye.
- abrupt onset of signs and symptoms will be present in stevens- johnson syndrome.it has poor prognosis .
- Leading questions can be asked in progressive condition.
- Dry eye states due to immune disorder tends to progress relentlessly, chronic recurrent pattern seen in ocular cicatricial pemphigoid
- Previous treatment history should be asked and any allergic reaction to that medications should be noted

a. **Patient symptoms**:

Eventhough symptoms alone not adequate for differential diagnosis of dry eye,they remain an important parameter of dry eye examination, , because the same symptoms can be perceived with a range of ocular surface conditions and tear film disorders.

Symptoms include—dryness, burning, itching ,grittiness, foreign body sensation, tiredness, redness, inability to keep the eye open and tearing. Tearing can occur in dry eye states, though paradoxical, due to the reflex tearing.

Decreased afferent secretion leads to Drying of the ocular surface.This

- stimulates the afferent receptors on the ocular surface leading to lacrimal gland secretions and reflex tearing .
- look for diurnal periodicity.progressive symptoms occurs in moderate dry eye because during sleep evaporation of tears will be reduced .
- In immune related dry eye,symptoms will be more during awakening.
- In meibomian gland inflammation- symptoms primarily in the morning.
- Ocular surface disorders-symptoms more on awakening.
- There are many symptoms based questionnere like OSDI (ocular surface disease index) to assess the dry eye.

So careful and detailed clinical history is extremely useful in classifying the etiologies of disease and directing treatment modalities.

b. **Occupational and medical history:**

The occupational environment of the patient forms an important role of history taking. Conditions that increase evaporation from the ocular surface such as constant exposure to low humidity,

air conditioned environment,

extremely hot and dry surroundings,

exposure to dust or chemical fumes should be noted.

A number of drugs could aggravate the dry eye state.

A few of these include antitussives ,antihypertensives, antihistamines, decongestants and antidepressants.

c. **Associated systemic disorders**:

A number of systemic disorders can aggravate the dry eye disease. very often, the ophthalmologist may be the first person to diagnose an underlying systemic disorder in patients presents with dry eye.

- Most common systemic cause for dry eye is Rheumatoid arthritis .so history of morning stiffness in the joints should be asked .
- Immune dysfunctional states can also alter the secretions of the other secretory glands resulting in dry mouth

- seborrheic dermatitis causes Meibomian gland dysfunction (dandruff) leads to tear film alteration.

d. **Importance of rapport building**:

History taking is not only important for assessing the severity and diagnosis, it is also important in for developing good rapport between the patient and doctor.Dry eye is a chronic condition for which there is no specific cure. Since this having psychological component also in it, it is essential for the patient to develop trust and confidence in the physician who is treating the patient.

It helps the physician to assess the profile of the patient, patient expectations from the treatment, and his understanding of the disease process.

e. contact lenses history should be asked . Howlong the patient is wearing the contact lens , contact lenses type and solutions using for cleaning the lens, whether the patient sleeps with the contact lenses and timing of symptoms relating to contact lens usage.

CLINICAL TESTS TO EVALUATE THE DRY EYE DISEASE

Tear Secretion Assessment

Schirmer's Test

Schirmer's test, , remains the most commonly employed technique for tear secretion assessment. It is performed by placing a sterile Whatman 41 ,35 × 5 mm folded filter paper strip ,over the lid margin at the junction of lateral one-third and

the medial two-third of the lower lid.amount of wetting portion in the filter paper is noted after 5 minutes in millimeters.

Schirmer’s 1:< 5 mm at 5 minutes is considered abnormal.

Schirmer’s 2:schirmer’1 with nasalstimulation.abnormal value is < 10mm at 5 minutes .

Abnormal value in both the tests is indication of lacrimal gland dysfunction .it affects both the normal ,and reflex tear secretion.

Schirmer's 3:Schirmer's 1 along with retinal stimulation by looking at the sun, not used at present.

Jones basal tear secretion

Same as schirmer’s I but before placing stripes anaesthetic drops should be applied.

Phenol Red Thread Test

1982 ,Hamano invented this phenol red thread tear test.

Phenol red impregnated cotton thread is inserted into the lateral side of the lower conjunctival sac for 15 seconds. , phenol red turns from yellow colour to bright orange When thread is wetted with tears and the length of thread wetted measures aqueous tear production.

If it is 9-18 mm of wetting then it is considered as normal. This test is more reliable and repeatable than the Schirmer's test.

Tear Volume Assessment

The lower tear film meniscus is examined for its height,, regularity, width and curvature.

The normal height of tear meniscus is 0.1-0.3 mm.

The presence of debris/ mucin and foam in the tear film along, the eyelid margin is suggestive of inflammation, and meibomian gland dysfunction respectively.

Reflective meniscometry-it projects, black and white stripes, and measures the curvature of the lower tear film meniscus, from this meniscus volume ,can be approximately calculated.

Radius of tear film meniscus curvature is directly proportional to volume of tear meniscus , and if the radius of the tear film curvature is less than 0.25 mm, then it indicates, hyposecretory dry eye.

Other noninvasive methods are optical coherence tomography,, strip meniscometry,, and a device Tearscope Plus using interference phenomena.

Tear Clearance Assessment

Tear Clearance Test

The fluorescein clearance test is a dynamic , tear functional test. It measures basic tearing, ,reflex tearing and tear clearance simultaneously.

This test is performed as follows:

- one drop of, 0.5 % proparacaine is applied to each eye , the inferior fornix is dried with tissue paper carefully.
- 5 µl of 0.25% fluorescein is instilled in the lower conjunctival cul-de-sac without touching the conjunctival surface.Then The patient is asked to blink normally.
- Schirmer's testing is carried out for about 1 minute at the end of 10, 20 and 30 minutes respectively.
- In the last test ,that is at the end of the 30 minutes, Schirmer strip is placed after nasal stimulation byusing cotton tipped applicator.
- If the dye cannot be detected ,at the 20-minute interval, then Clearance is defined as normal.

Its clinical applications are:

1. To determine aqueous tear deficiency , with higher accuracy.

2. To differentiate dry eye into with or without reflex tearing.

primary lacrimal gland diseases or Sjögren syndrome are characterized by the loss of reflex tearing, thus helping to establish the severity of dry eye.

3. To guide the physicians to perform punctal occlusion with plugs or, permanent cauterization.

4. To determine, subclinical dry eye which is a cause of ocular irritation, medicamentosa and other ocular surface disorders.

Fluorophotometry

Fluorophotometric techniques can be used for quantitating tear secretion and volume. But it is expensive and technique lacks standardization.

Tear Function Index (TFI)

This test is similar to the Schirmer test with anesthesia, but involves the addition of 10 drops of 0.5 % fluorescein. Five minutes after instillation, the length of the wetted portion is measured and the intensity of dye staining is compared to the standard strip colors.

The TFI value, is equal to the value of the Schirmer test with anesthesia divided by the Tear clearance rate.

TFI=SCHIRMER'S TEST/TCR

The tear clearance rate is proposed, as a simple and useful method to estimate tear flow ,basal tear turnover and measure tear drainage indirectly. It is calculated with tear fluorophotometry, after instilling one drop of 2% of fluorescein and collecting the specimen. The disappearance of tear fluorescein is recorded over a period of 30 minutes. It shows a biphasic curve, which allows calculation of tear clearance rate.

low TFI value is seen in Patients with aqueous tear deficiency and delayed tear clearance .

Evaluation of Tear Film Stability

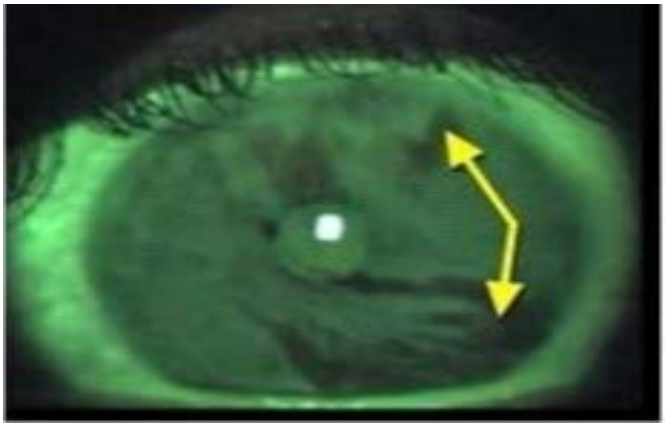
Tear Break-up Time

An unstable tear film ,is the hallmark of dry eye.There are Invasive and noninvasive techniques to assess the stability of the tear film.Tear film stability is measured by the tear break-up time (TBUT) test.It is the most important ,and practical test for diagnosing dry eye.

It is performed by placing fluorescein strip wetted with saline in the lower conjunctival sac , ask the patient to blink,and examine under the cobalt blue filter in the slit lamp.The time interval between a last complete blink and the first randomly appearing dry spot in the precorneal tear film should be noted.

This should be done without using topical anesthesia ,andwithout holding the lids. Tear film break-up may be initiated by the rupture of the mucous layer at

its thinnest spots, allowing the aqueous to come in contact with exposed patches of epithelium., This test is inaccurate and not reproducible.but it is most commonly used test clinically.



Noninvasive Tear Break-up Time

An another method, reflects a regular pattern off the corneal surface and measures the time for it to distort or breakup following a blink. fluorescein is not required, so this test is called noninvasive break-up time(NIBUT).

Other methods for determining the NIBUT

- Xeroscope,
- the Keeler tearscope,
- Placido-based computerized videokeratoscopy.

A value of > 10 sec is considered normal for both TBUT and NIBUT, reflects tear film instability, whereas less than 5 seconds is a marker of definite dry eye.

The tear breakup pattern:

lipid layer deficiency- linear on the inferior and central cornea aqueous tear deficiency.- more random circular breakup pattern over areas of punctate epitheliopathy

Lipid Layer Assessment

Meibomian gland dysfunction

The following are signs of meibomian gland dysfunction

a) ductal orifice metaplasia -white shafts of thickened meibum in the orifices

b) reduced expressibility of meibomian gland secretions

c) increased turbidity and viscosity of the expressed secretions

d) dropout of glandular acini

Ocular Surface Damage Assessment

(1) Diagnostic Dye Staining*:* Three types of dyes are used in ocular surface damage assessment.They are fluorescein, rose-bengal, and lissamine green and they assess the following,

• Integrity of the ocular surface epithelium

• Protective status of the precorneal tear film.

Fluorescein dye*:*

It assess the intactness of the epithelial barrier.stains only if cellular membrane disrupts or cell-cell junction loss present

Pseudostaining may occur when fluorescein dye pools in indented, healthy epithelium.

Rose-bengal dye-It stains both devitalized epithelial cells and healthy epithelial cells which are not protected by a normal mucin layer. Before using rose Bengal dye topical anesthetic should be instilled since it is irritating.

Rose bengal stains the conjunctiva more intensely than the cornea but in severe cases of dry eye,it can stain the entire cornea.

Lissamine green*:* Lissamine green is a synthetic organic acid dye .it stains the ocular surface similar to Rose Bengal but it does not cause irritation. It detects dead or degenerated cells .It does not stain healthy conjunctival epithelium.

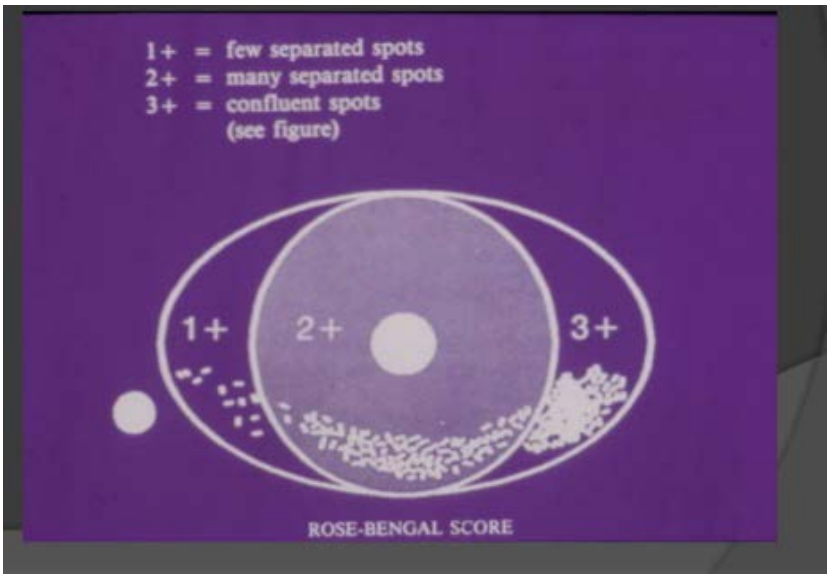
Interpretation of staining is based on :

- intensity
- location.

Different grading schemes for ocular surface dye staining have been proposed as follows, but a universal grading scheme is yet to be finalized.

a. **van Bijstervald staining**

   It uses rose-bengal for staining of the conjunctiva and cornea. It divides the ocular surface into 3 quadrants, the nasal and temporal triangular areas of conjunctiva and the cornea.each area is given the scale of 0-3 with a maximum score of 9. A score of more than 3 is considered abnormal.



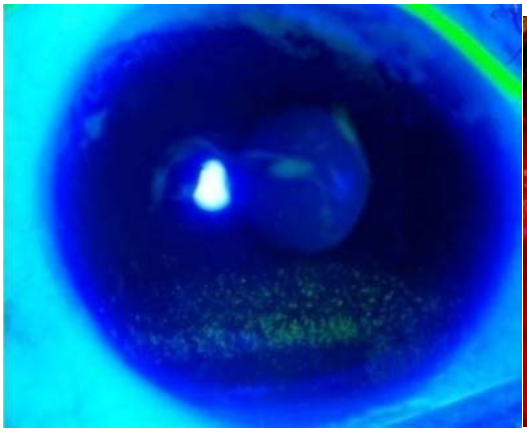
b. **Oxford scheme**-stains both the conjunctiva and cornea together using fluorescein and rose-bengal or lissamine green stain.It

c. uses a chart with a series of panels labeled A-E in order of severity (absent, minimal, mild, moderate,severe).

PANEL	GRADE	CRITERIA
A	0	Equal to or less than panel A
B	I	Equal to or less than panel B, greater than A
C	II	Equal to or less than panel C, greater than B
D	III	Equal to or less than panel D, greater than C
E	IV	Equal to or less than panel E, greater than D
>E	V	Greater than panel E

c. **The NEI workshop grading system***:* It uses fluorescein to grade the cornea and rose-bengal for conjunctiva.It divides the cornea into 5 areas and conjunctiva 6 areas.each area is given the score of 0-3 depending upon the severity. A score of > 3 out of 15 and >3 out of 18 is considered abnormal for the cornea and conjunctiva respectively.

Though no specific grading system can be considered superior to the other, the aim is to remain consistent in technique and grading over time.

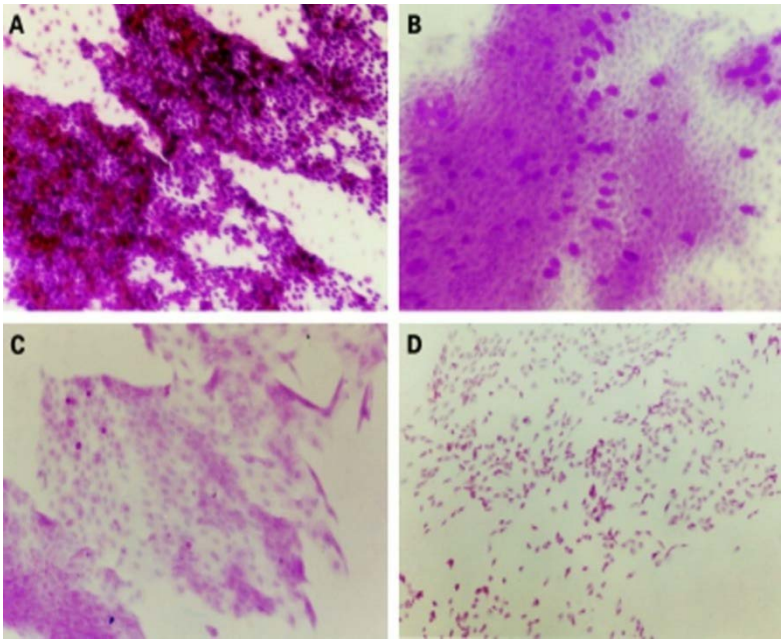


(2) Impression Cytology*:* It has been useful in the investigation of many aspects of dry eye disease such as:

• Pathophysiology of dry eye (degree of squamous metaplasia)

• Monitoring clinical trials (to evaluate efficacy of treatments)

• Associating dry eye disease with other systemic conditions.



Based on the cellular changes occurring in the course of squamous metaplasia,dry eye is graded as

Stage 0-normal cellular structures

Stage 1-early loss of goblet cells without keratinization

Stage2-Total loss of goblet cells with slight enlargement of epithelial cells

Stage3-early and mild keratinization

Stage4-moderate keratinization

Stage5-Advanced keratinization

(3) Tear Osmolarity*:* In dry eye, there is impaired balance between tear secretion, evaporation and clearance leads to an increase in tear osmolarity, which is considered one of the major sources of discomfort, ocular surface damage and inflammation.

Its cut-off value is 315.6 mOsmol/L between healthy and dry eyes.

(4) Tear protein assays.

(5) Corneal sensitivity*:* Cochet-Bonnet esthesiometer, uses a monofilament nylon which is extendable from 0-60 mm.

When applied perpendicularly to the corneal surface with a bending angle of 5 degrees, this thread exerts pressures from 11-200 mg/mm2 correlating inversely with the length of the filament.

Two types noncontact esthesiometers:

- gas esthesiometer and
- noncontact esthesiometer.

Clinically,a cotton wick can be used to assess corneal sensation.

Management

Aims to be achieved are:

- To improve the patient's ocular comfort and quality of life,
- Maintain the normal homeostasis of ocular surface and tear film

Although symptoms can rarely be eliminated, they can be improved, leading to an improvement in the quality of life.

Management of dry eye includes

- avoidance of exacerbating factors
- eyelid hygiene
- tear supplementation,
- tear retention,
- tear stimulation, and
- Anti-inflammatory agents.
- Surgical procedures

Avoidance of Exacerbating Factors

Environmental modifications

- humidification,
- avoidance of wind or drafts
- avoidance of dusty or smoky environments

Lifestyle or workplace modifications,

- taking regular breaks from prolonged reading or computer use,
- lowering the computer monitor below eye level so that the gaze is directed downward.
- Increasing blink frequency or fast blinking exercise

Eyelid Hygiene

The conventional treatment of meibomian gland dysfunction consists of warm compresses, lid hygiene, topical and systemic antibiotic, topical steroids and artifical tears.

Tear Supplementation

Ocular lubricants are mainstay of dry eye treatment. These products differ with respect to number of variables, electrolyte composition, osmolarity or osmolality, and presence or absence of preservatives and compatible solutes.

The ideal artificial lubricant should be

- preservative-free,
- contain potassium, bicarbonate and other electrolytes
- have a polymeric system to increase its retention time.
- neutral to slightly alkaline pH.
- Osmolarities of artificial tears - 181 to 354 mOsm/L.

Higher artificial tear viscosity increases the retention time and may help to protect the ocular surface.

Viscosity agent used in artificial tears :

- carboxymethylcellulose,
- polyvinyl alcohol
- , propylene glycol
- hydroxypropyl-guar

High viscosity agents tend to cause blurring of vision, therefore low viscosity agents are generally preferred for mild to moderate dry eye.

Preservatives in the artificial tears retard the growth of microbial organisms but also usually have toxic effects on the ocular surface.

The most commonly employed preservatives :

benzalkoniumchloride,chlorobutanol, thimerosal and chlorhexidine, benzalkonium chloride is the most toxic one.

Benzalkonium chloride is the most frequently used preservative in topical ophthalmic preparations, as well as in topical lubricants.

Preferred preservatives include sodium chlorite which degrades to chloride ions and water upon exposure to Ultra violet light after instillation and sodium perborate which is converted to water and oxygen on contact with the tear film.Tear substitutes with preservatives are usually well tolerated in mild dry

eye,but if more frequent use is necessary, preservative free tear substitutes are recommended.

In general, ointments do not require preservatives ,so do not support bacterial growth .Gels containing high molecular weight crosslinked polymers of acrylic acid (carbomers) have longer retention times than artificial tear solutions, but have less visual blurring effect than petrolatum ointments.

Tear Retention

Indicated in aqueous-deficient dry eye .In aqueous deficiency, tear clearance should be lowered by means of Lacrimal outflow occlusion. Before doing punctual occlusion,The presence of ocular surface inflammation needs to be identified because, occlusion of tear outflow would prolong contact of the abnormal tears containing proinflammatory cytokines with the ocular surface. So inflammation can worsen following punctal occlusion Therefore, treatment of inflammation before plug insertion has been recommended.

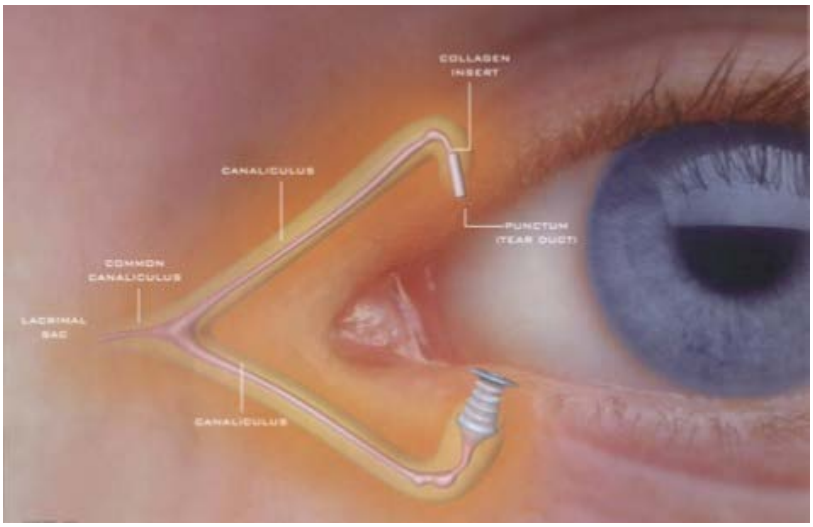
Punctual occlusion done by thermal method, by implanting plugs or by surgical methods.

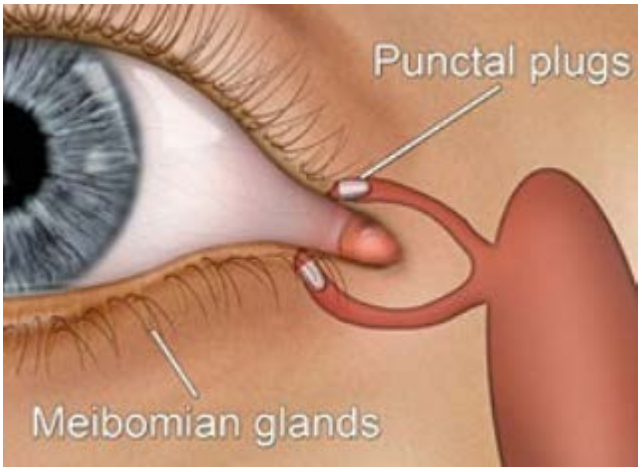
1. **Punctal occlusion:**The aim of punctal occlusion is to retard tear clearance in an attempt to treat the ocular surface of patients with deficient aqueous tear production.

Punctal plugs are divided into the following types:

• **Absorbable**: Made of collagen or polymers. Theocclusion duration ranges from 7-180 days.The plugs dissolve by themselves or may be removed by saline irrigation.

Nonabsorbable: Made of silicone or hydrophilic acrylic, are intended to be permanent





Contraindications to the use of punctal plugs :

- allergy to the materials used in the plugs to be implanted,
- punctal ectropion

- pre-existing nasolacrimal duct obstruction, which would presumably, negate the need for punctal occlusion.

complication of punctal plugs:

spontaneous plug extrusion-most common

more troublesome complications -internal migration of a plug,

- biofilm formation

- infection

- pyogenic granuloma formation.

2. **Moisture chamber spectacles**: They reduce tear evaporation by increasing humidity around the eye.

3. **Contact lenses**- retain the tear film and

promote ocular surface healing.

4. Tarsorrhaphy*:* It is done to narrow the palpebral aperture, decreasing evaporation. If partial closure fails, complete closure may be indicated.

Tear Stimulation:

Secretagogues

Several potential topical pharmacologic agents may stimulate aqueous secretion, mucous secretion or both. The agents currently under investigation are

- diquafosol (one of the P2y2 receptor agonists)
- rebamipide,

- gefarnate,
- ecabet sodium-mucous secretion stimulants

Two orally administered cholinergic agonists, pilocarpine and cevilemine

Biological Tear Substitutes

1. **Autologous serum tears:**Autologous serum tears have biochemical and mechanical properties similar, but not identical, to those of normal aqueous tears. They are unpreserved but can be stored frozen for 3 to 6 months, so that blood donation is required 2 to 4 times a year.

Effective in severe or refractory dry eye. These are usually well tolerated and most patients report improvement of discomfort sensation.

Rare side effects- increased discomfort, slight epitheliopathy, bacterial conjunctivitis or eyelid eczema.

2.Autologous platelet rich plasma*:*

Platelet-rich plasma contains high numbers of platelets that produce growth factors. They induce mesenchymal and epithelial cells to migrate and proliferate. It has a lubricating effect.

2. **Salivary gland autotransplantation:**

Salivary submandibular gland transplantation is capable of replacing deficient mucin and the aqueous tear film phase. It reduces ocular discomfort but no useful in vision.

Anti-inflammatory Therapy

Based on the concept that inflammation is a key factor in the pathogenesis of dry eye, the efficacy of a number of anti-inflammatory agents for treatment of dry eye disease has been evaluated. These include:

1. **Topical cyclosporine:** Topical cyclosporine is currently the only pharmacologic treatment that is FDA approved specifically for dry eye. Cyclosporine is disease modifying agent.

   It reduces conjunctival IL-6 levels, decreases activated lympocytes in the conjunctiva, reduces conjunctival inflammatory and apoptotic markers, and increases conjunctival goblet cell numbers.

2. **Corticosteroids**

   Topical corticosteroids are effective but they are generally recommended only for shortterm use because prolonged use might result in adverse effects including ocular infection, glaucoma and cataracts.

3. **Oral tetracyclines:** Tetracyclines are used in dry eye primarily for their anti-inflammatory rather than antibacterial actions.

   Mechanisms may include

   - Decreased matrix metalloproteinase activity
   - decreased production of proinflammatory cytokines such as interleukin (IL)-1 and tumor necrosis factor-alpha.

Essential Fatty Acids

They benefit dry eye in two ways:

By reducing inflammation and by altering the composition of meibomian lipids. There are at least two EFA nutritional supplements marketed specifically for DED: omega-3 fatty acids from flax seed and fish oil

blend of omega- 3 and omega-6 fatty acids from cod liver oil.

Omega-6 fatty acids are precursors for arachidonic acid and certain proinflammatory lipid mediators prostaglandin E2 and Leukotriene B4.but, certain omega-3 fatty acids inhibit the synthesis of these lipid mediators and block production of IL-1 and TNF-alpha.

Higher omega-6:omega-3 ratio was associated with significantly greater DED risk.

The International Dry Eye WorkShop (DEWS) Subcommittee members reviewed the Delphi Panel (the Dry Eye Preferred Practice Patterns of the American Academy of Ophthalmology and the International Task Force Delphi Panel on Dry Eye) approach to the treatment of dry eye and modified it.

Treatment recommendations are based on disease severity of DED:

• **Level 1**

- Education and environmental/dietary modifications
- Elimination of offending systemic medications
- Preserved artificial tear substitutes, gels and ointments
- Eyelid therapy (for MGD).

• **Level 2**— If level 1 treatment is inadequate, the following is to be added:

- Nonpreserved artificial tear substitutes
- Anti-inflammatory agents

 Topical corticosteroids

 Topical cyclosporin A.

- Topical/systemic omega-3 fatty acids
- Tetracyclines -for meibomian gland disease
- Punctal plugs should be considered after control of inflammation
- Secretagogues
- Moisture chamber spectacles.

• **Level 3—**If level 2 treatment is inadequate, the following are recommended:

- Autologous serum eye drops
- Contact lenses
- Permanent punctal occlusion.

• **Level 4**—If level 3 treatment is inadequate, add the following:

- Systemic anti-inflammatory agents
- Surgery

 Lid surgery

 Tarsorrhaphy

 Mucous membrane grafting

 Salivary gland duct transposition

 Amniotic membrane transplantation

Final Outcome of Dry Eye Disease

If the dry eye is left untreated,the following complications will occur,

• Ocular surface related

– Punctate epitheliopathy

_Epithelial defect.

– Erosions

- Patient related

– Visual effects

increased blink rate dueto rapid tear breakup time leading degradation of image

– Symptom related, ocular fatigue dueto subjective distress

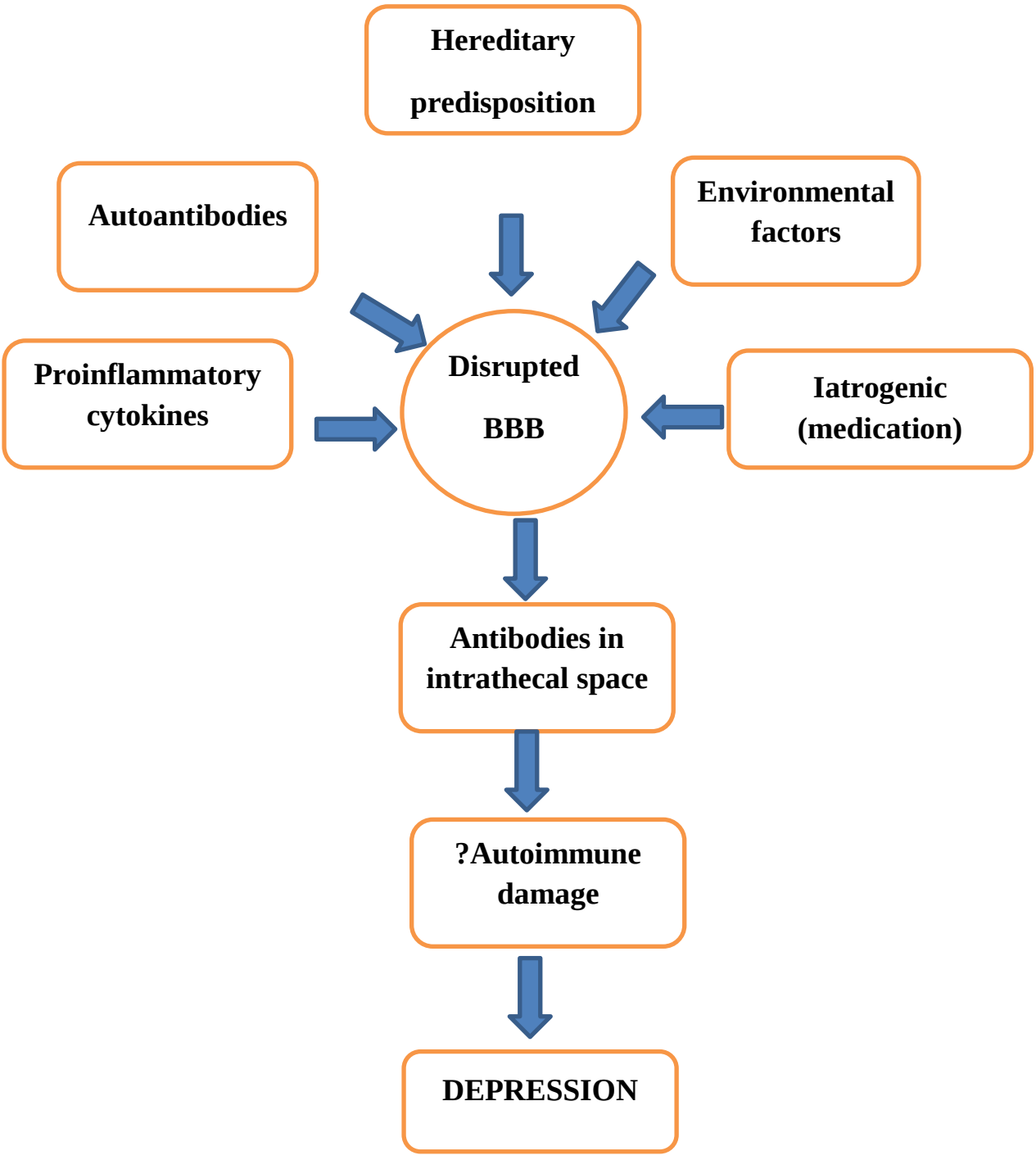
Sterile melting

Bacterial keratitis

DEPRESSION

Depression is a life threatening disorder which affects hundreds of millions of people all over the world.any age can be affected from childhood to late life.it causes sever distress and disruption of life.if left untreated it can be fatal.It is estimated that by the year 2020 if current trends for demographic and epidemiological transition continue, it would be the second leading cause of disability-adjusted life years (DALYs)

The main mechanism in depression is decreased levels of serotonin, norepinephrine, and dopamine.


Hereditary predisposition
Autoantibodies
Environmental factors
Proinflammatory cytokines
Disrupted BBB
Iatrogenic (medication)
Antibodies in intrathecal space
?Autoimmune damage
DEPRESSION

All these factors causes release of pro inflammatory cytokines IL-alpha,TNF –alpha,IL-6 will activates HPA axis leads to impaired neurotransmitter system especially serotonin.

There are many studies saying that depression and dry eye disease are associated with each other.

Studies mentioned that depression and DED have common pathophysiological mechanisms

1)an increase in the production of inflammatory cytokines IL-1,IL-6 and TNF seen in both diseases and increase in the saturated to polyunsaturated fatty acid ratio in DED and depression.

2)Both disease have common risk factors such as menopause and female gender

3)serotonin receptors have been discovered in the conjun ctival epithelium,and similarly ,mRNAs of receptors for serotonin were found in mouse meibomian glands

4)neurotransmitters released in the vicinity of the gland influence the meibomian gland secretions to the ocular surface.so disturbances in this system could lead to disturbances in ocular surface which could explain the dry eye in depression.

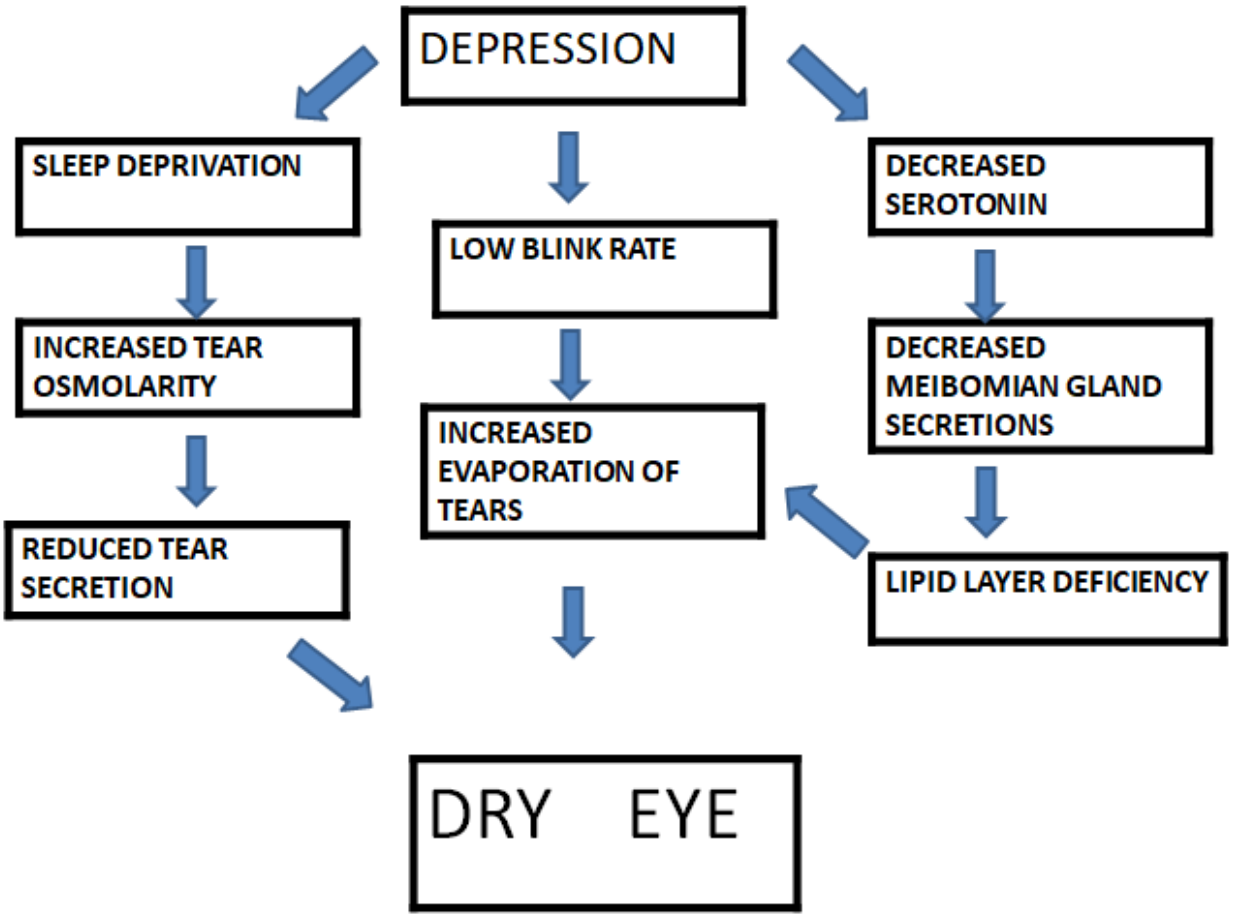
5)Study by martin and Brennan says that serotonin was identified in human tears and lead to an increased chloride secretion by the cornea.so lack of serotonin causes dysfunction of the corneal epithelium.

Nesime et al study concluded that reduction of TBUT and moderate ocular surface damage was seen in depressive patients.

- Low blink rate in depression patients lead to increased evaporation of tears which causes dry eye
- Decreased impulses to efferent parasympathetic secretomotor fibres in depressive patients leads to decreased secretion of tears from lacrimal gland
- Sleep deprivation in depressive patients will lead to

  1) increased tear osmolarity

  2)decreased tear secretion



So all the above studies says that there is strong association between DED and depression with anxiety disorder .

So it is important to determine the association between DED and depressive disorder and it is very crucial to determine the severity of DED in such patients for treatment purposes and to reduce the ocular complications.

REVIEW OF LITERATURE

A cross sectional study of dry eye disease in newly diagnosed depressive disorder patients on 36 patients with 32 control group was conducted by nesime et al at turkey recently and they concluded that prevalence is more in depression patients than controls.

A retrospective case control study of The Association Between Dry Eye Disease and Depression and Anxiety in a Large Population-Based Study conducted by weaver et al in 460611 patients which includes 7207 patients with dry eye ,20 004 patients with anxiety and 30 100 patients with depression and concluded that there is strong association between dry eye disease and depression and anxiety disorder.

A cross sectional study of Dry Eye Disease in Patients With Depressive and Anxiety Disorders in Shanghai done in 472 psychiatric patients including 176 patients (37%) with depression, 170 patients (36%) with generalized anxiety disorder, 60 patients (13%) with depression and anxiety disorder, 55 patients (12%) with obsessive–compulsive disorder, and 11 patients (2%) with panic disorder and DED was present in 283 patients (60%).

PART II

TITLE

“AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLY DIAGNOSED DEPRESSIVE DISORDER PATIENTS ’’

AIM&OBJECTIVES

To Determine the Prevalence of the dry eye disease in newly diagnosed depression patients without any previous medication.

STUDY DESIGN

- Cross sectional observational study

SAMPLE SIZE: 100 patients

MATERIALS AND METHODS:

- Newly diagnosed depressive disorder patients from psychiatry Department at Government Rajaji Hospital, Madurai.

STUDY CENTRE

- Department of ophthalmology and Department of Psychiatry ,Government Rajaji Hospital,Madurai.

STUDY PERIOD

- 6 months

Inclusion criteria:

- Age >18 and <70years
- Newly diagnosed depressive disorder patients without any previous medication

Exclusion criteria:

- Age<18 years >70 years
- Depressive disorder patients on drugs
- Ocular infections, inflammatory patients
- Patients taking anti hypertensives, antihistamines, anti tussives, antiandrogens, topical eye drops
- Contact lens wearers
- Previous H/O ocular surgeries

- H/O auto immune disorders
- Pregnancy
- Thyroid disorder
- Lid anomalies(ectropion,entropion,lagophthalmos,trichiasis)

METHODOLOGY:

- All subjects will be selected only after they provide informed consent for entry into the trial.
- The newly diagnosed depression disorder patients with no history of medication will be selected from psychiatry department.
- All patients are diagnosed and classified as mild,moderate,severe depression on the basis of ICD 10 Classification for depressive disorder by the psychiatrists.
- On the same day, All patients shall undergo a complete ocular examination like visual acuity by snellen‘s chart,Tntraocular pressure,fundus examination, dry eye tests like tear film break up time(TBUT), Tearfilm meniscal height, ocular surface staining with fluorescein, schirmer’s test, slit lamp biomicroscopic examination of eyelid margins and meibomian gland orifices, expression of meibum secretions .Blink rate also is measured.

- Tear film meniscus height should be measured by slit lamp examination.
- Tear film break up time -measured after impregnated fluorescein 1mg strip and placed in the lateral one third of the lower eyelid. The interval between the last complete blink and the appearance of first dry spot in the stained tear film is measured.
- For ocular surface evaluation, fluorescein strips are used by applying saline to moisten the strips and wet strips applied to the inferior palpebral conjunctiva.
- After 15 secs stained area in the conjunctiva are examined and compared with oxford scoring panel ,then according to that severity is graded.
- Schirmer's test is performed by placing a sterile 35*5mm folded Whatman41 filter paper strip over the lid margin at the junction of the medial two third and lateral one third of lower lid.
- after 5 minutes the length of wetting strips should be recorded in millimeters. Values less than 10mm at 5 minutes is considered as abnormal.
- Dry eye is said to be present if minimum 2 tests are positive.

- Since there was no significant difference between Right and Left eye TBUT,Schirmer's score,TFMH,Oxford score I took Right eye values for statistical purposes.

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer by using SPSS 16 software.

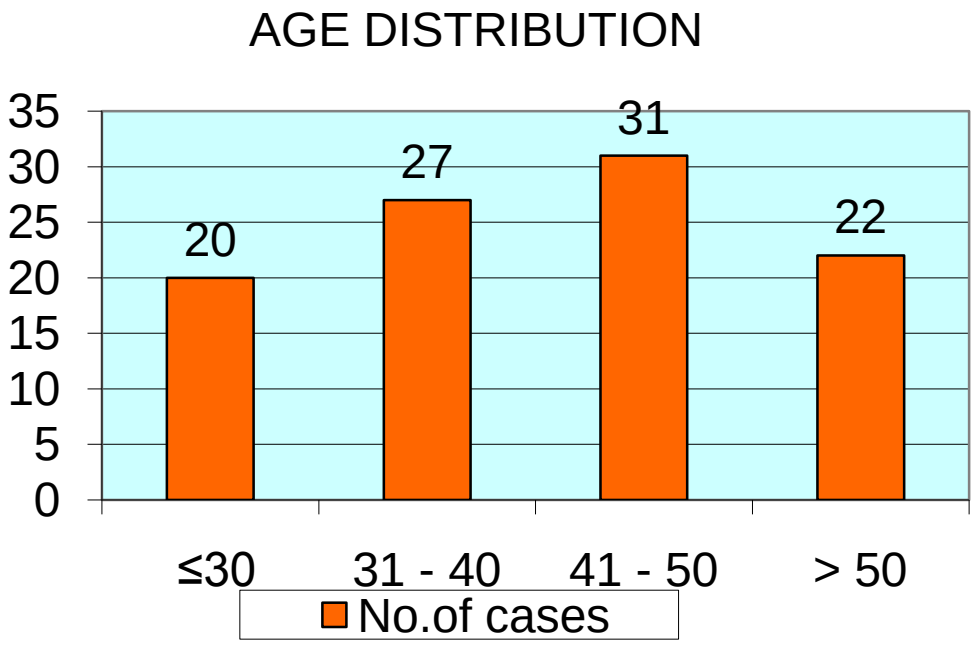
Using this software, 'p' values were calculated through chi square test for consolidated data to test the significance of difference between variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS AND INTERPRETATION:

AGE DISTRIBUTION

Of the studied 100 population ,20(20%)were less than 30 years of age,27(27%)between 31-40 years,31(31%) between 41-50 years,22 (22%) persons at more than 50 years of age.

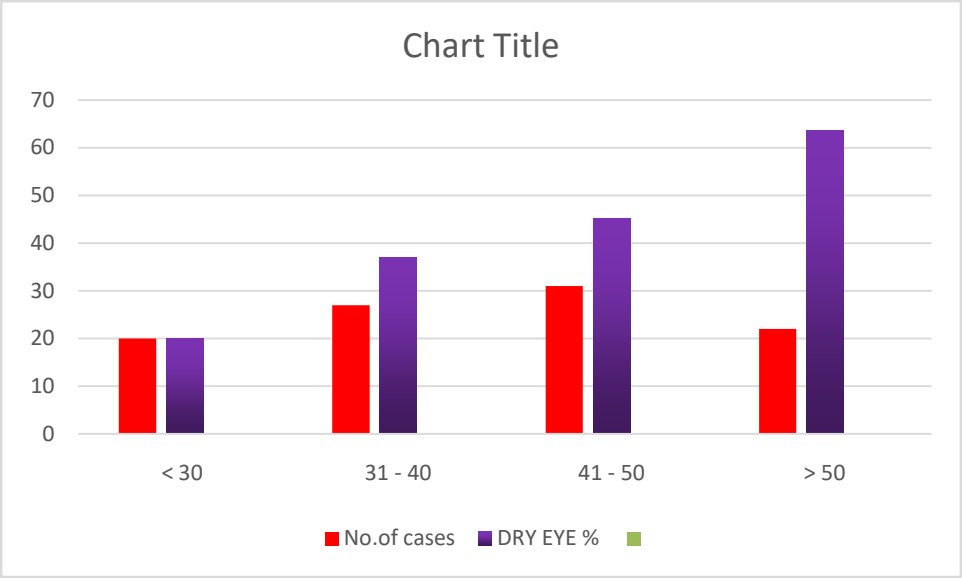
Age in years	No.of cases
≤30	20
31 - 40	27
41 - 50	31
> 50	22
Total	100



AGE VS DRY EYE

Of the 100 studied population,only 4 patients(20%) had dry eye in <30 years of age group, 10 (37%) had dry eye in 31-40years of age, 14 (45.2%) developed dry eye in 41-50 years of age,14(63.6%) showed dry eye in >50 years of age group.

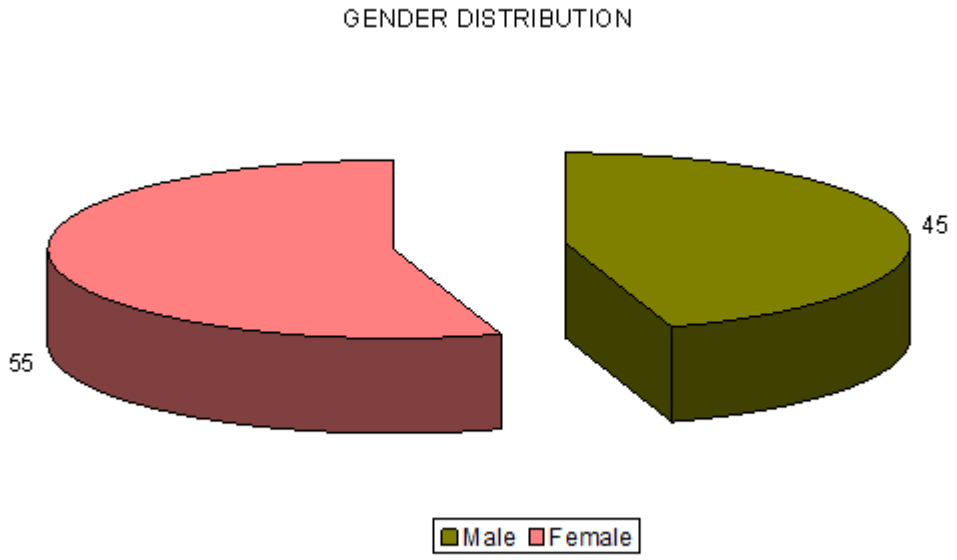
Age in years	No.of cases	DRY EYE	DRY EYE %
< 30	20	4	20
31 - 40	27	10	37
41 - 50	31	14	45.2
> 50	22	14	63.6



SEX DISTRIBUTION

Among the 100 studied population 45% were males and 55 %were females.The study showed depression is more in female gender as in literature.

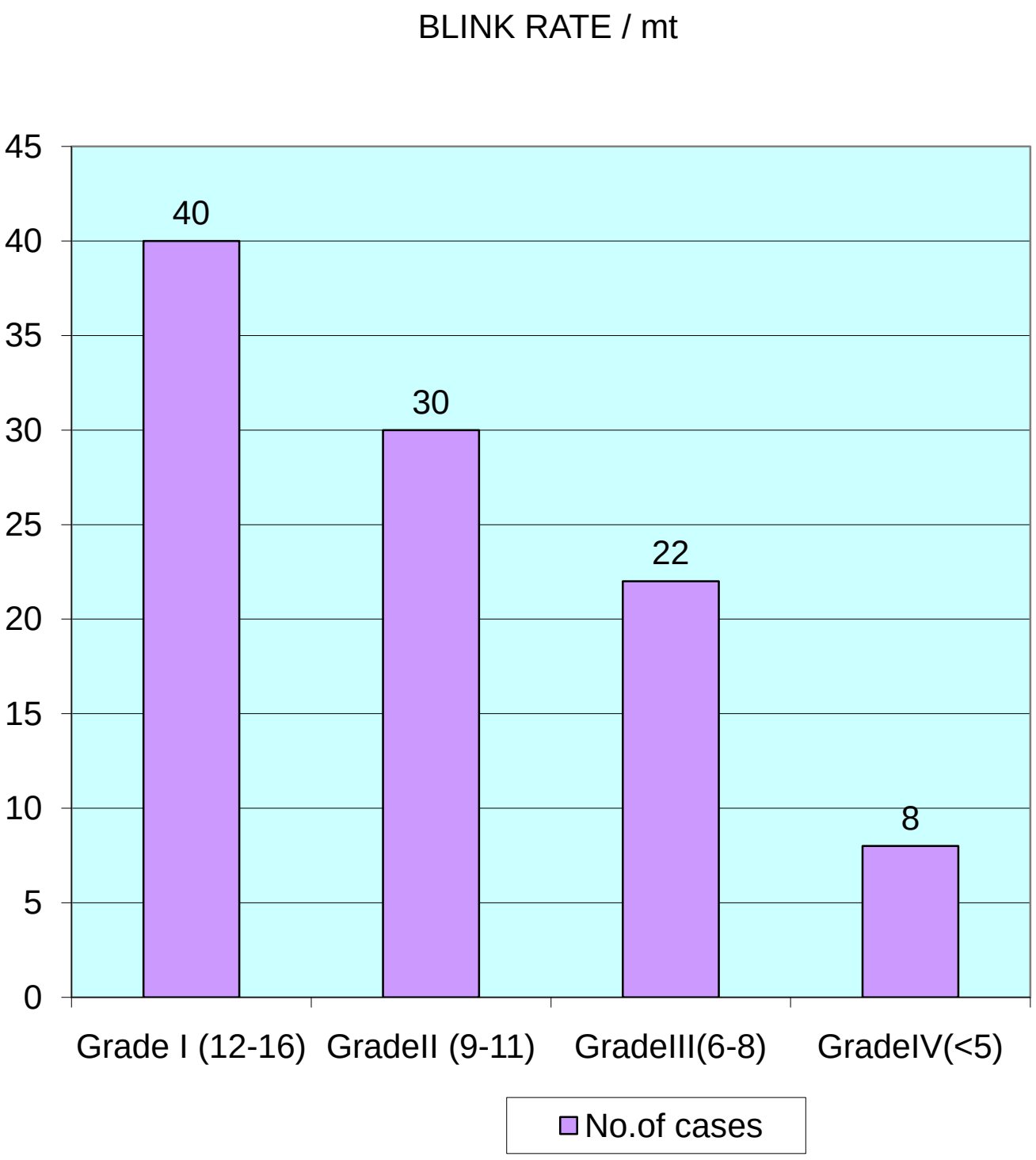
Gender	No.of cases
Male	45
Female	55
Total	100



BLINK RATE DISTRIBUTION

BLINK RATE/ mt	No.of cases
Grade I(12-16)	40
Grade II (9-11)	30
Grade III (6-8)	22
Grade IV (≤5)	8

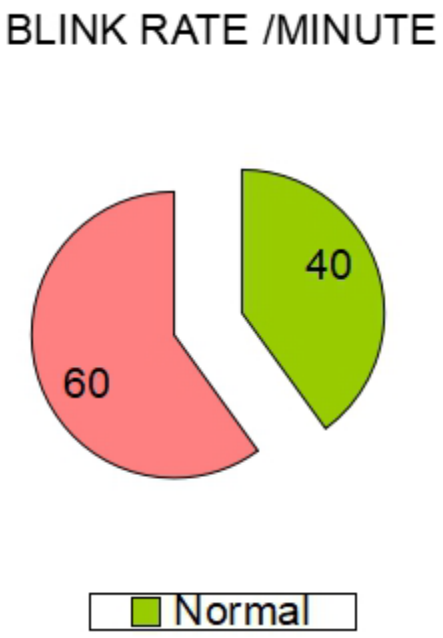
Of the 100 studied population,40% had normal blink rate,30% had Grade II(75% of normal),22% had GradeIII(50% of normal),8% had GradeIV(25% of normal) blink rate.


BLINK RATE / mt
45
40
35
30
25
20
15
10
5
0
40
30
22
8
Grade I (12-16)
GradeII (9-11)
GradeIII(6-8)
GradeIV(<5)
No.of cases

BLINK RATE INTERPRETATION

Among 100 study population ,40 patients(40%) had normal blink rate and 60 patients(60%) had abnormal blink rate.it correlates with that depression patients have lower blink rate.

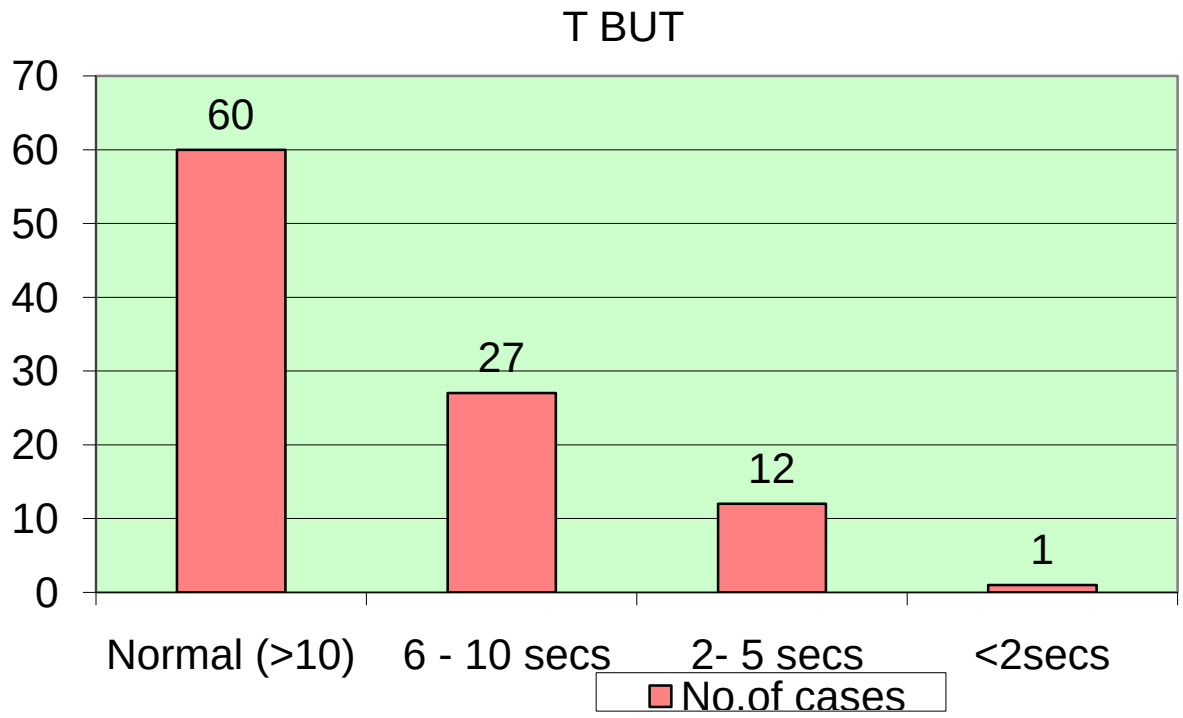
BLINK RATE/ mt	No.of cases
Normal	40
Abnormal	60
Total	100



TEAR FILM BREAKUP TIME DISTRIBUTION

Of 100 population,60 persons had normal TBUT (>10 secs),27 had 6-10 secs,12 had 2-5 secs,only one person showed <2 secs of TBUT.

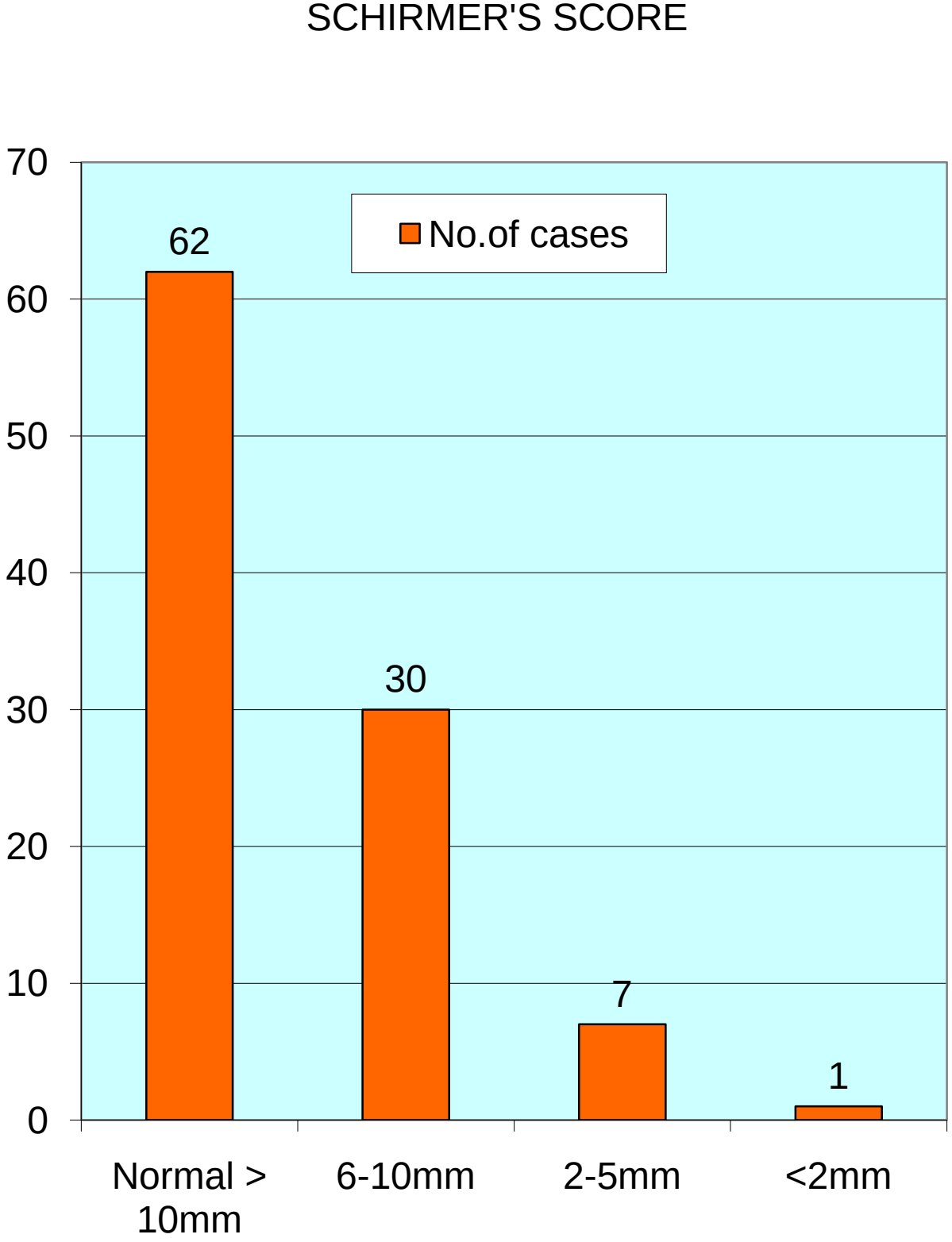
T BUT(secs)	No.of cases
Normal (>10)	60
6 - 10 secs	27
2- 5 secs	12
<2secs	1
Total	100



SCHIRMER'S SCORE DISTRIBUTION

Of 100 studied population,62 patients had normal schirmer's score (>10 mm/5 mts),30 had 6-10 mm,7 patients had 2-5 mm,1 patient had <2 mm score.

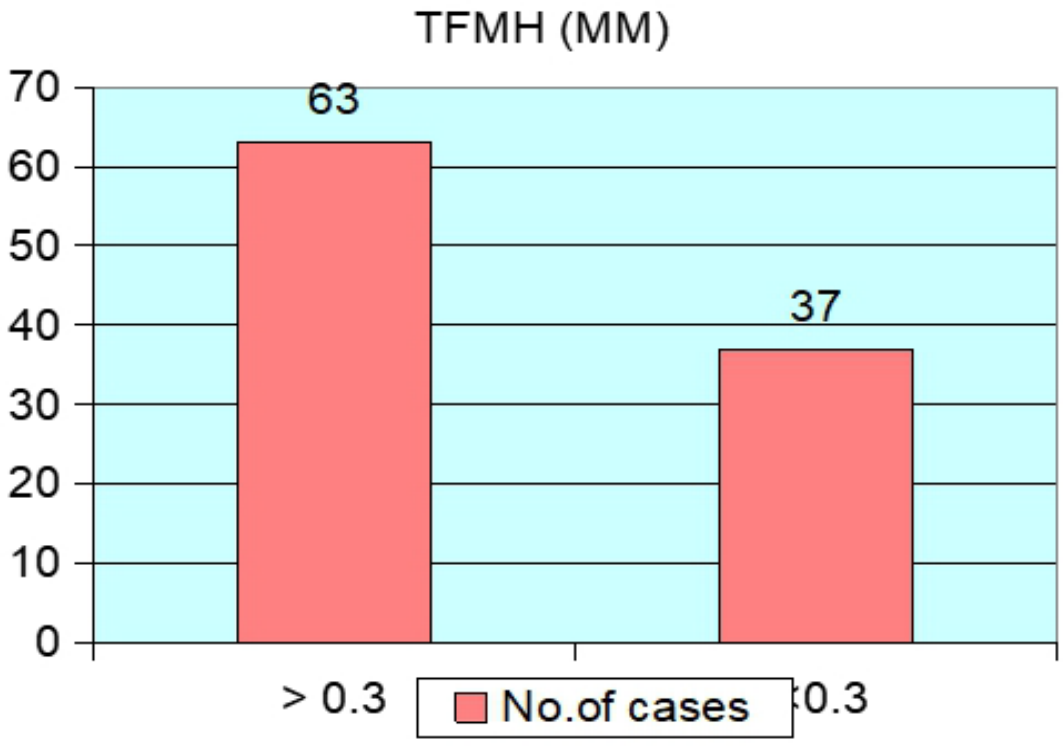
SCHIRMER'S I SCORE	No.of cases
Normal > 10mm	62
6-10mm	30
2-5mm	7
<2mm	1
Total	100


SCHIRMER'S SCORE
70
60
50
40
30
20
10
0
No.of cases
62
30
7
1
Normal > 10mm
6-10mm
2-5mm
<2mm

TEAR FILM MENISCAL HEIGHT

Among 100 studied population,63 patients showed >0.3 mm height of TFMH which is normal,and 37 patients showed <0.3 mm of TFMH.

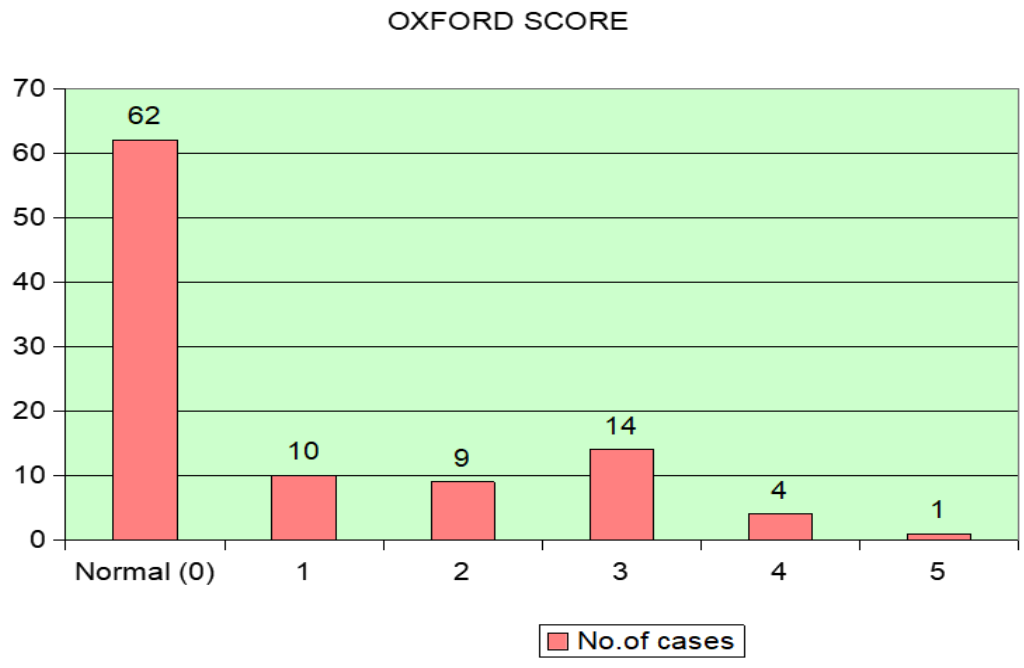
TFMH(mm)	No.of cases
< 0.3	37
> 0.3	63
Total	100



OXFORD SCORING

Of 100 population,62 patients showed normal oxford score,10 had grade 1,9 patients showed grade 2,14 showed grade 3,4 persons showed grade 4,only one person showed grade 5 which is severe dry eye.

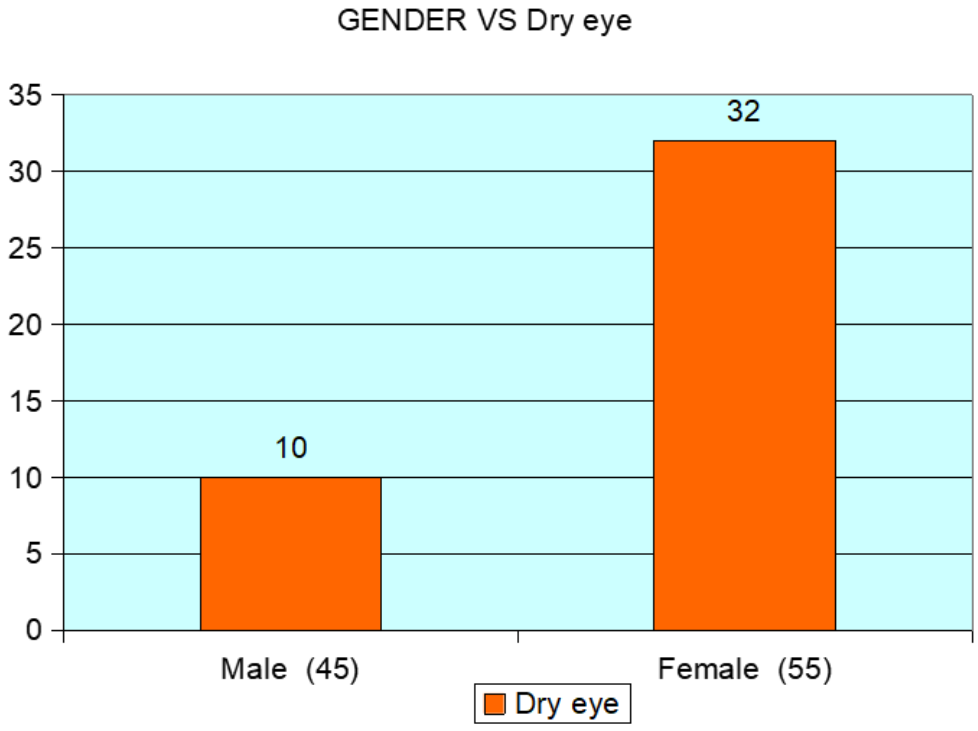
oxford score	No.of cases
Normal (0)	62
1	10
2	9
3	14
4	4
5	1
Total	100



GENDER VS DRY EYE

Among 45 studied male patients,10 (22.2%) had dry eye disease, whereas in 55 (58.2%) studied female patients 32 had dry eye disease which is statiscally significant(p value 0.029.).

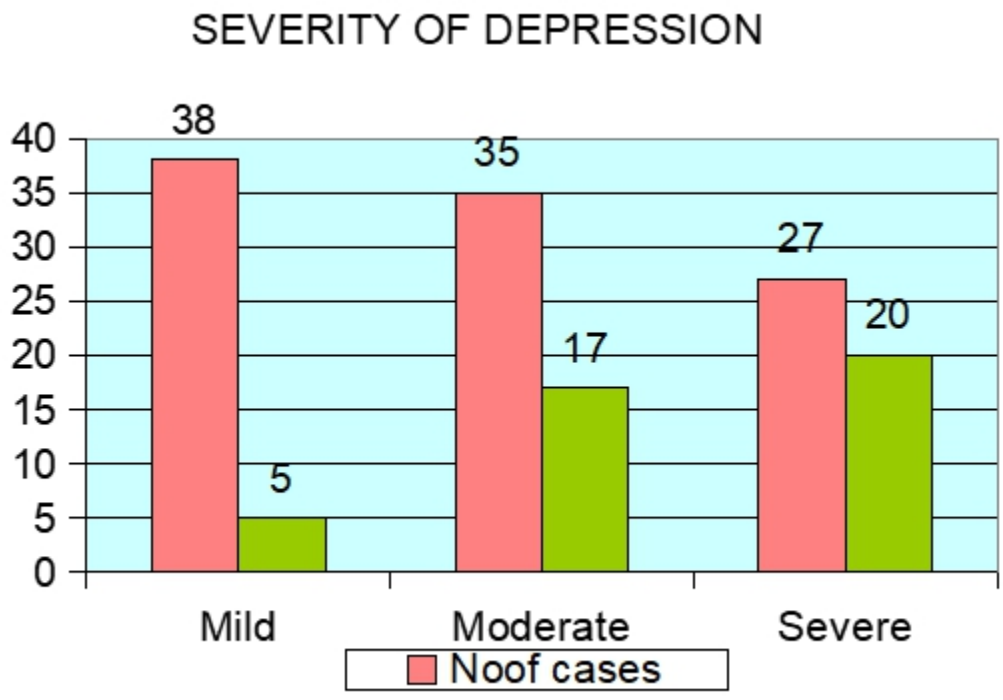
Gender vs Dry eye	Dry eye
Male (45)	10
Female (55)	32
Total	42
P VALUE	0.029 Stastically significant



SEVERITY OF DEPRESSION VS DRY EYE

Of the 100 studied population,38 patients belongs to mild depression group,35 belongs to moderate depression,27 had severe depression.In that 38 patients 5 (13.2%) patients had dry eye,in 35 patients 17(48.6%) had dry eye,and in 27 patients 20(74.1%) had dry eye.

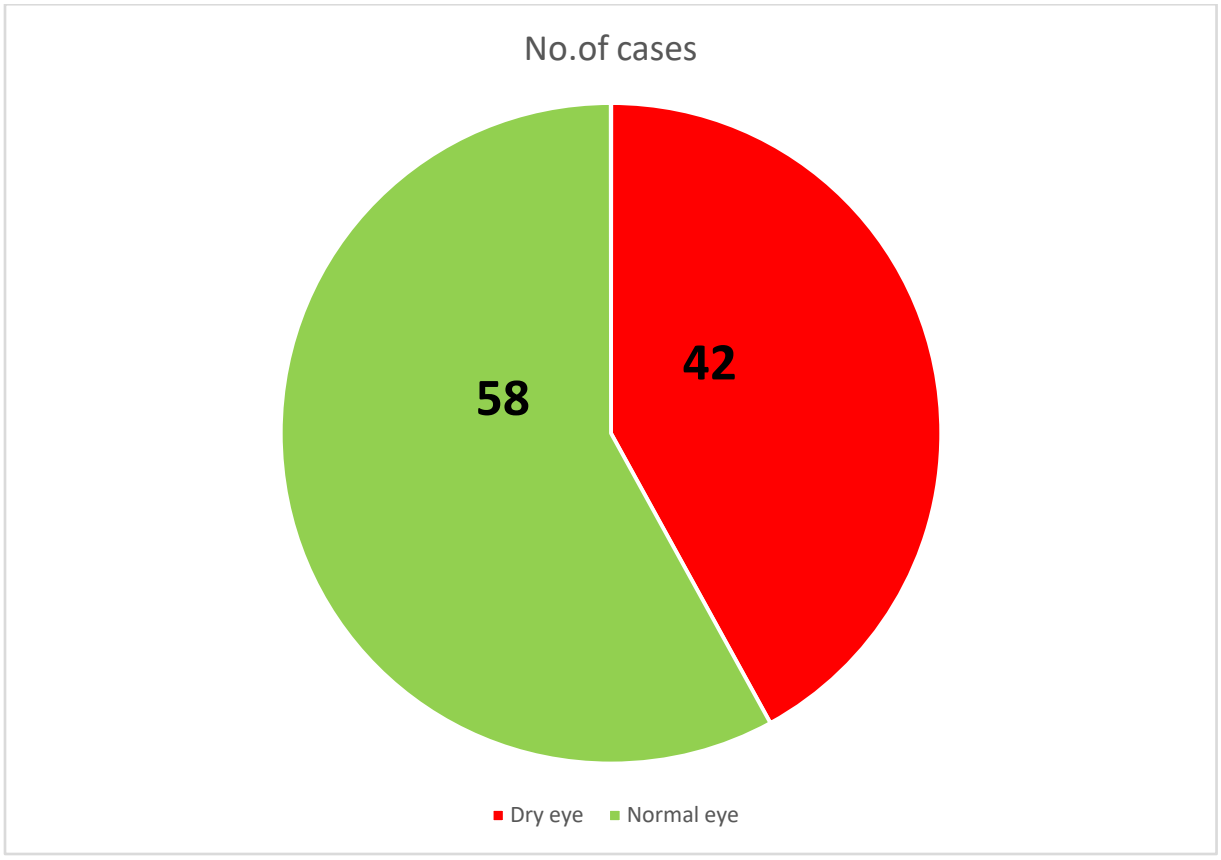
Severity of depression	No of cases	No.of dry eye
Mild	38	5
Moderate	35	17
Severe	27	20



PREVALENCE OF DRY EYE

Among 100 studied population,42% had dry eye,58% did not have dry eye.The prevalence of dry eye disease is 42%.

Study population	No.of cases
Dry eye	42
Normal eye	58
Total	100

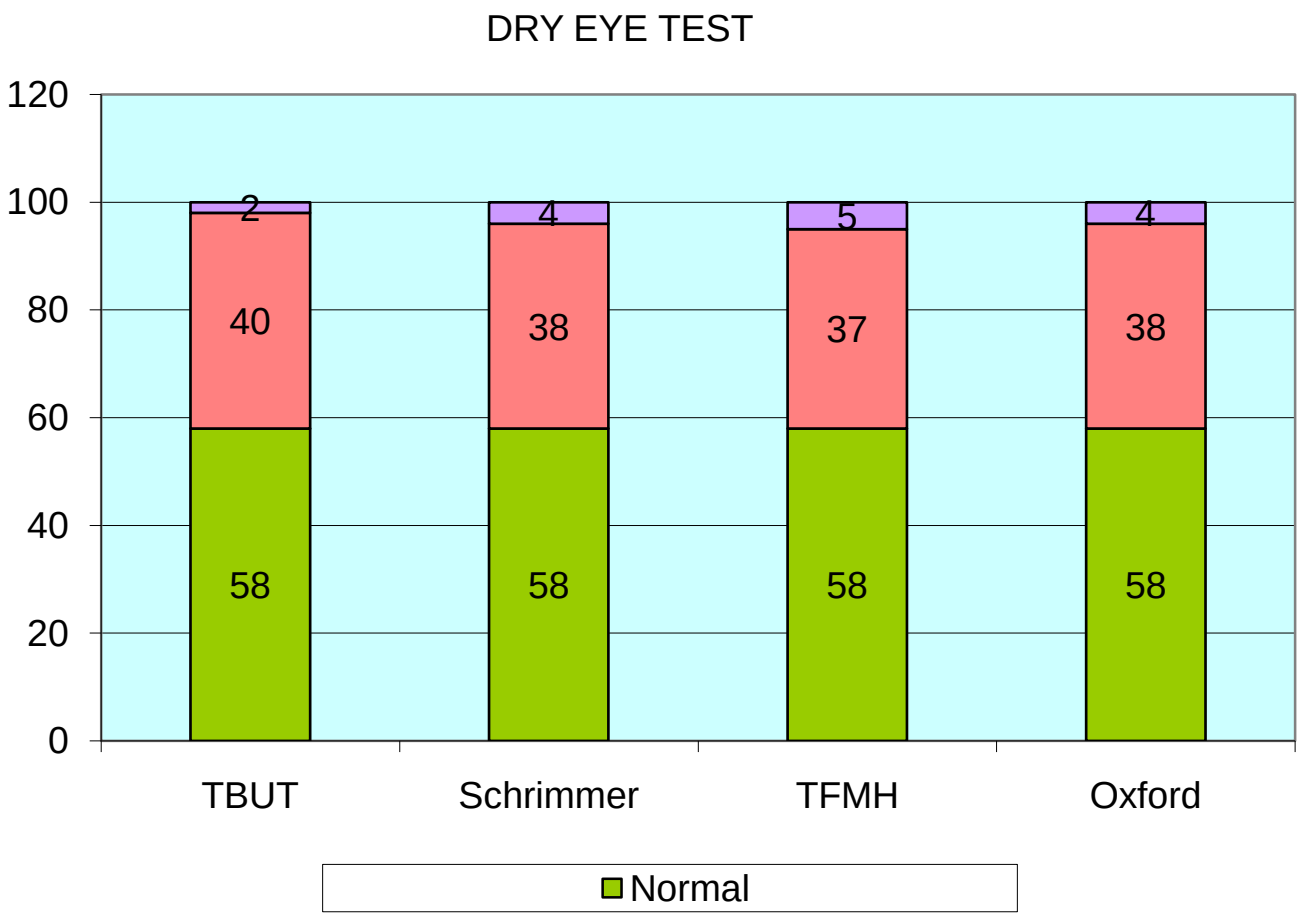


DISTRIBUTION OF DRY EYE DISEASE IN VARIOUS TESTS

Of 100 patients dry eye disease is positive in 42 patients .Among 42 patients,32 showed positive in all the 4 tests,5 patients showed positive in 3 tests,5 showed 2 tests positive.

Among 4 type of dry eye tests TBUT positive in 40 cases,schirmer's positive in 38 cases,TFMH positive in 37 cases,Oxford score positive in 38 patients.

	Normal	Positive cases	Positive in other tests
TBUT	58	40	2
Schirmer's score	58	38	4
TFMH	58	37	5
Oxford score	58	38	4


DRY EYE TEST
120
100
80
60
40
20
0
2
40
58
4
38
58
5
37
58
4
38
58
TBUT
Schrimmer
TFMH
Oxford
Normal

SUMMARY

This study was an observational study to determine the incidence and prevalence of the dry eye disease in newly diagnosed depressive disorder patients without any previous medication. . All the patients included in inclusion criteria were selected and dry eye tests are done in all 100 patients.

AGE DISTRIBUTION

Of the studied 100 population ,20 were less than 30 years of age,27 between 31-40 years,31 between 41-50 years,22 persons at more than 50 years of age.

AGE VS DRY EYE

>50 years of age group showed 63.6% of dry eye disease which correlates with literature as prevalence is more in advanced age.

SEX DISTRIBUTION

55 patients from our study were females which also correlates with literature as prevalence of depression is more in female gender.

BLINK RATE DISTRIBUTION

In our study, 60% of the studied population had abnormal blink rate which shows that depressive patients have low blink rate.

TEAR FILM BREAKUP TIME DISTRIBUTION

Of 100 population,60 persons had normal TBUT (>10 secs),27 had 6-10 secs,12 had 2-5 secs,only one person showed <2 secs of TBUT.

SCHIRMER'S SCORE DISTRIBUTION

Of 100 studied population,62 patients had normal schirmer's score (>10 mm/5 mts),38% had low schirmer's score.

TEAR FILM MENISCAL HEIGHT

Among 100 studied population,63(63%) patients showed normal TFMH,and 37(37%) patients showed low TFMH.

OXFORD SCORING

Of 100 population,62 patients showed normal oxford score,38% showed abnormal oxford score.

GENDER VS DRY EYE

Among 45 studied male patients,10(22.2%) had dry eye disease whereas in 55 studied female patients 32 (58.2%) had dry eye disease which is statiscally significant(p value 0.029)and it correlates well with literature as like depression ,dry eye also more common in female gender.

PREVALENCE OF DRY EYE

Among 100 studied population,42% had dry eye,58% did not have dry eye.so the prevalence of dry eye disease in depression patients in our study is 42%.

DISTRIBUTION OF DRY EYE DISEASE IN VARIOUS TESTS

Among 4 type of dry eye tests TBUT positive in 40 cases,schirmer's positive in 38 cases,TFMH positive in 37 cases,Oxford score positive in 38 patients.all the 4 tests identified the disease almost equally.

DISCUSSION

Dry Eye Disease (DED) is a huge problem among people nowadays. Its prevalence rate is 5-34%. Dry eye disease is a common public health problem in the modern era with multifactorial etiology.. The study about dry eye disease is a rapidly expanding field nowadays , which requires the ophthalmologist to stay abreast because of diagnostic challenges that mimic, coexist with dry eye and newer management modalities . All the age groups are affected sothat causing considerable impact on the health sector both in terms of finances, manpower,because it not only affects the quality of vision but also affects the quality of life. Our aim is to treat the symptoms and prevent the ocular complications.

Increased Prevalence rate is seen with age, contact lens wear, male sex, , ophthalmic surgeries, current smoking history and with coexisting ocular conditions like blepharitis, meibomian gland dysfunction, pterygium, , and conjunctival disease. Dry eye disease is also seen in patients with arthritis, thyroid dysfunction and poor general health.

Some Research says that DED is more common in women than in men particularly in the age of 50-52 years that is at menopausal age group. Because in menopausal age ,there is an imbalance between androgen and oestrogen hormones

which are necessary for the formation of lipid layer.so deficiency of these hormones may lead to dry eye.

Similarly in our study ,prevalence is more common in female patients at the age of >50 years.

If Dry eye is not evaluated for its risk factors, It leads to an economic burden to the patients and it may cause delay in the treatment. The quality of life of the people will be affected in terms of daily visual acuity.It also causes social stigma because the irritation and other symptopms of the dry eye will lead to chronic red eye .so Patient may land up in depression and anxiety disorder.

Like Dry eye disease ,Depression also a major public health importance, in view of its dysfunction,prevalence , morbidity, and economic burden.

There are some Recent studies, which reported an association between depression and dry eye and post-traumatic stress disorder,anxiety and dry eye.

Wen et al(2012) conducted a study in 472 psychiatric patients includes depression and anxiety and concluded that increased frequency of dry eye was present in that patients.

Galor et al also demonstrated the association between dry eye and depression.

In our study the prevalence is 42% which correlates with literature of, Nandi et al 1992 .

A large population-based study was conducetd recently, in Chennai.In that study more than 24,000 subjects are included using Patient Health Questionnaire (PHQ)-12 and results were analysed for prevalence of depression and it was 15.1% after age adjustments using 2001 census data.

In 1992, Nandi et al did a study in the same area which compared the prevalence of depression and reported that the prevalence was increased from 49.93 cases per 1000 population to 73.97 cases per 1000 population.

So many Studies were conducted in primary care clinics/center have estimated a prevalence rate of 21-40.45%.

In this study dry eye is more(63.6%) in elderly(>50years) patients when compared to the younger one similar to the Beijing Eye study.

weaver et al did a study in a large population to analyse the association between dry eye disease and depression and anxiety disorders and concluded that there is strong association between dry eye and depressive disorder.

The relationship between depression and DED remains unclear. The pain which occurs in dry eye disease may induce the depression.

Antidepressants which are used in the treatment of depression are also involved in the pathogenesis of DED.

But some studies says that not only the anti depressants causing dry eye ,even the newly diagnosed depressive disorder patients without any medication also get dry eye disease .

On November 2016, nesime et al conducted a study at turkey.They evaluated the prevalence of the dry eye disease in patients diagnosed to have depression who were not on any treatment .

They explained the mechanism behind this was due to some serotonin receptors which are found in conjunctiva and nearby to the meibomian glands.this serotonin receptors are involved in the secretion of tear fim.so deficiency of these receptors which occurs in depression could explain the cause for dry eye disease.

The inflammatory cytokines which are involved in the depression also involved in the dry eye disease.

In our study ,42 patients among 100 studied population developed dry eye disease.it shows that dry eye disease will occur in even newly diagnosed depression patients also and not the anti depressants alone causing the dry eye.

.CONCLUSION

So, From this study it is clearly seen that the depression itself causing dry eye disease,not only the anti depressants which are using for treating the depression.If we do not diagnose the dry eye early and not properly treated ,they may go for serious complications like corneal melting,perforation etc and eventually vision loss.So, it is important that psychiatrists take this into account especially while prescribing anti depressants which also aggravates dry eye disease and send the patients for ocular screening for dry eye disease once they diagnose the depression ,to avoid such complications and to improve the quality of life.

PART III

BIBILIOGRAPHY

1. The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007).Ocul Surf 2007;5:75-92.
2. Gayton JL. Etiology, prevalence and treatment of dry eye disease. ClinOphthalmol 2009;3:405-12.
3. The epidemiology of dry eye disease: Report of the Epidemiology Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:93-107.
4. Lambert DW, Foster CS, Perry HD. Schirmer test after topical anesthesia and the tear meniscus height in normal eyes. Arch Ophthalmol 1979;97:1082-5.
5. Connor CG, Flockencier LL, Hall CW. The influence of gender on the ocular surface. J Am OptomAssoc 1999;70:182-6.
6. Krenzer KL, Dana MR, Ullman MD, Cermak JM, Tolls DB, Evans JE, *et al*. Effect of androgen deficiency on the human meibomian gland and ocular surface. J ClinEndocrinolMetab 2000;85:4874-82.
7. Wolkoff P, Nøjaard JK, Troiano P, Piccoli B. Eye complaints in the office environment: Precorneal tear film integrity influenced by eye blinking efficiency. Occup Environ Med 2005;62:4-12.

8. Management and therapy of dry eye disease: Report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf 2007;5:163-78.
9. Dana MR, Hamarah P. Role of immunity and inflammation in corneal and ocular surface disease associated with dry eye. AdvExp Med Biol 2002;506:729-38.
10. Hamarah P, Haq SO, Gulati A, Dana MR. Mechanism of ocular surface immune response. In: Pflugflelder SC, Roger W.B, editors. Dry eye and Ocular Surface disorders. New York: Marcel Dekker; 2004. p. 111-41.
11. Zoukhri D. Effect of inflammation on lacrimal gland function. Exp Eye Res 2006;82:885-98.
12. Zhu Z, Stevenson D, Ritter T, Schechter JE, Mircheff AK, Kaslow HR, *et al*. Expression of IL-10 and TNF-inhibitor genes in lacrimal gland epithelial cells suppresses their ability to activate lymphocytes. Cornea 2002;21:210-4
13. American Academy of Ophthalmology. Punctal occlusion for the dry eye. Three-year revision. ophthalmic procedure assessment. Ophthalmology 1997;104:1521-4.
14. Pflugfelder SC. Antiinflammatory therapy for dry eye. Am J Ophthalmol 2004;137:337-42.

15. Rosenberg ES, Asbell PA. Essential fatty acids in the treatment of dry eye. Ocul Surf 2010;8Suppl 1:18-28
16. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop. (2007). Ocul Surf 2007;5(2):75–92.
17. Wang TJ, Wang IJ, Hu CC, Lin HC. Comorbidities of dry eye disease: a nationwide population-based study. Acta Ophthalmol 2012;90(7):663–668.
18. Shah S, Jani H. Prevalence and associated factors of dry eye: our experience in patients above 40 years of age at a Tertiary Care Center. Oman J Ophthalmol 2015;8(3):151–156.
19. Li M, Gong L, Chapin WJ, Zhu M. Assessment of vision-related quality of life in dry eye patients. Invest Ophthalmol Vis Sci 2012;53(9):5722–5727.
20. Sun X. Dry eye disease in patients with depressive and anxiety disorders in Shanghai. Cornea 2012;31(6):686–692.
21. Fraunfelder FT, Sciubba JJ, Mathers WD. The role of medications in causing dry eye. J Ophthalmol 2012;2012:285851.
22. Martin XD, Brennan MC. Serotonin in human tears. Eur J Ophthalmol 1994;4(3):159–165.
23. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea 2003;22(7):640–650.

24. Kim KW, Han SB, Han ER, Woo SJ, Lee JJ, Yoon JC, et al. Association between depression and dry eye disease in an elderly population. Invest Ophthalmol Vis Sci 2011;52(11):7954–7958.

25. Li M, Gong L, Sun X, Chapin WJ. Anxiety and depression in patients with dry eye syndrome. Curr Eye Res 2011;36(1):1–7.

26. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.

27. Labbé A, Wang YX, Jie Y, Baudouin C, Jonas JB, Xu L. Dry eye disease, dry eye symptoms and depression: the Beijing Eye Study. Br J Ophthalmol 2013;97(11):1399–1403.

28. Wen W, Wu Y, Chen Y, Gong L, Li M, Chen X, et al. Dry eye disease in patients with depressive and anxiety disorders in Shanghai. Cornea. 2012;31(6):686–692. doi: 10.1097/ICO.0b013e3182261590. [PubMed]

29. Walt JG, Rowe MM, Stern KL. Evaluating the functional impact of dry eye: the Ocular Surface Disease Index. Drug Inform J. 1997;31:1436.

30. Ahmet A, Bayram C. The Depression Anxiety and Stress Scale (DASS): The Study of Validity and Reliability. Educ Sci Theory Pract. 2007;7(1):260–268.

31. Wang TJ, Wang IJ, Hu CC, Lin HC. Comorbidities of dry eye disease: a nationwide population-based study. Acta Ophthalmol. 2012;90(7):663–668. doi: 10.1111/j.1755-3768.2010.01993.x. [PubMed]

32. Li M, Gong L, Sun X, Chapin WJ. Anxiety and depression in patients with dry eye syndrome. Curr Eye Res. 2011;36(1):1–7. doi: 10.3109/02713683.2010.519850. [PubMed]

33. Li MY, Gong L, Chapin WJ, Zhu M. Assessment of Vision-Related Quality of Life in Dry Eye Patients. Invest Ophthalmol Visual Sci. 2012;53(9):5722–5727. doi: 10.1167/Iovs.11-9094. [PubMed]

34. Galor A, Feuer W, Lee DJ, Florez H, Faler AL, Zann KL, et al. Depression, Post-traumatic Stress Disorder, and Dry Eye Syndrome: A Study Utilizing the National United States Veterans Affairs Administrative Database. Am J Ophthalmol. 2012;154(2):340–346. doi: 10.1016/j.ajo.2012.02.009. [PubMed]

35. Nesime Setge Tiskaoglu, Alper Yazıcı, Tunay Karlıdere, Esin Sari, Elif Yilmaz Oguz, Musa Musaoglu, show all Dry Eye Disease in Patients with Newly Diagnosed Depressive DisorderPages 672-676 | Received 06 Mar 2016, Accepted 11 Sep 2016, Published online: 21 Nov 2016.

ABBREVIATIONS

DED -DRY EYE DISEASE

DEWS-DRY EYE WORKSHOP

NEI -NATIONAL EYE INSTITUTE

TFI-TEAR FUNCTION INDEX

TCR-TEAR CLEARANCE RATE

TBUT-TEAR BREAKUP TIME

NIBUT-NON INVASIVE TEAR BREAKUP TIME

TFMH-TEARFILM MENISCAL HEIGHT

ICD-10-INTERNATIONAL CLASSIFICATION OF DISEASE

PROFORMA

NAME: **AGE:** **SEX: M / F**

ADDRESS: **PHONE NUMBER:**

DATE :

SOCIOECONOMIC HISTORY

CHIEF COMPLAINTS

H/O PRESENTING ILLNESS

PAST MEDICAL AND SURGICAL HISTORY

TREATMENT HISTORY

FAMILY HISTORY : Yes ☐ No ☐

PERSONAL HISTORY

MENSTRUAL HISTORY

SEVERITY OF DEPRESSION

GENERAL EXAMINATION

BUILT-

NOURISHMENT-

ORIENTATION-

PARAMETERS	RE	LE
UCVA		
BCVA		

OBLIQUE EXAMINATION OF EYES

RIGHT EYE	STRUCTURE EXAMINED	LEFT EYE
	LIDS	
	CONJUCTIVA	
	CORNEA	
	ANTERIOR CHAMBER	
	IRIS	
	PUPILS	
	LENS	

SLIT LAMP EXAMINATION

RIGHT EYE	STRUCTURE EXAMINED	LEFT EYE
	LIDS-LID MARGINS EYE LASHES MEIBOMIAN GLAND ORIFICES	
	CONJUCTIVA	
	CORNEA	
	ANTERIOR CHAMBER	
	IRIS	
	PUPILS	
	LENS	

INTRAOCULAR PRESSURE AS MEASURED BYGOLDMANN APPLANATION TONOMETRY

	RIGHT EYE	LEFT EYE
BLINK RATE/mt		
TBUT(secs)		
TEAR FILM MENISCAL HEIGHT(mm)		
SCHIRMER'S TEST		
OXFORD SCORE		

DILATED FUNDUS EXAMINATION

RIGHT EYE		LEFT EYE
	MEDIA	
	DISC	
	CUP-DISC RATIO	
	VESSELS	
	AV RATIO	
	MACULA	
	FOVEAL REFLEX	

S.NO	NAME	AGE(Yrs)	SEX	UCVA		SEVERITY OF DEPRESSI	BLINK RATE/ mt	TBUT(secs)	SCHIRMER'S I SCORE(m	TFMH(mm)	oxford score	Dry eye
				RE	LE							
1	Raman	40	M	6/12	6/9p	MILD	10	12	15	>0.3	0	NO
2	selvi	35	F	6/6	6/6p	MODERATE	16	15	25	>0.3	0	NO
3	kandhasamy	45	M	6/18	6/12	SEVERE	11	14	20	>0.3	0	NO
4	valli	31	F	6/9	6/6	MODERATE	8	8	10	<0.3	2	yes
5	murugan	36	M	6/6p	6/9	MODERATE	9	14	24	>0.3	0	NO
6	Rasu	51	M	6/18	6/24	MILD	14	9	9	>0.3	0	yes
7	Jothi	46	F	6/6p	6/12	MODERATE	7	16	20	>0.3	0	NO
8	Pitchai	55	M	6/18	6/24	SEVERE	5	5	4	<0.3	3	yes
9	Mahalakshn	25	F	6/6	6/6	MILD	16	12	14	>0.3	0	NO
10	Kathammal	41	F	6/6	6/9	MILD	6	6	7	<0.3	0	yes
11	Shanmugam	52	M	6/36	6/18	MODERATE	12	16	15	>0.3	0	NO
12	Anand	27	M	6/6	6/6	MILD	14	14	25	>0.3	0	NO
13	Parvathy	45	F	6/9p	6/6	MODERATE	16	15	16	>0.3	0	NO
14	Seeniyamm	52	F	6/18	6/9	MODERATE	8	9	6	<0.3	1	yes
15	Jayakodi	29	F	6/6p	6/6	MILD	6	6	12	<0.3	0	yes
16	Meenakshi	42	F	6/24	6/12	MILD	10	12	15	>0.3	0	NO
17	Azhagu	46	F	6/18	6/36	SEVERE	5	5	5	<0.3	3	yes
18	Subramaniy	58	M	6/60	6/18	SEVERE	7	7	9	<0.3	3	yes
19	Meena	30	F	6/6	6/6	MODERATE	11	12	15	>0.3	0	NO
20	Saravanan	28	M	6/6p	6/9	MILD	10	15	16	>0.3	0	NO
21	kaveri	35	F	6/6p	6/6	MILD	9	12	20	>0.3	0	NO
22	kadhar huss	45	M	6/9p	6/18	MODERATE	11	12	18	>0.3	0	NO
23	shanthi	32	F	6/6	6/6	MODERATE	6	9	8	<0.3	2	yes
24	subbaiah	36	M	6/12	6/6	MILD	15	15	25	>0.3	0	NO
25	mariammal	51	F	6/18p	6/9	MODERATE	6	6	11	<0.3	2	yes
26	rakku	44	F	6/24p	6/18	SEVERE	4	4	3	<0.3	3	yes
27	kalirajan	37	M	6/6p	6/9	MILD	9	15	20	>0.3	0	NO
28	rose	25	F	6/6	6/6	MODERATE	14	12	30	>0.3	0	NO
29	alphoxia	42	F	6/9p	6/9	SEVERE	8	6	9	<0.3	4	yes
30	ganapathy	27	M	6/6	6/6	MILD	16	12	16	>0.3	0	NO
31	periyapandi	58	M	6/60	6/36p	MODERATE	12	14	25	>0.3	0	NO
32	vishwanthi	24	F	6/9	6/6p	MILD	16	15	16	>0.3	0	NO
33	Lakshmi	34	F	6/6	6/18	MODERATE	14	11	16	>0.3	0	NO
34	Selvaraj	34	M	6/6	6/6p	MILD	9	13	22	>0.3	0	NO
35	Sheela	42	F	6/36	6/18	MODERATE	15	12	15	>0.3	0	NO
36	Sasikala	50	F	6/9p	6/12	MILD	7	7	10	>0.3	0	yes
37	manjakalai	58	M	5/60	6/18	MILD	10	14	25	>0.3	0	NO
38	rathika	26	F	6/6p	6/18	MODERATE	8	9	7	<0.3	1	yes
39	Nagu	35	F	6/18	6/24	SEVERE	5	5	4	<0.3	3	yes
40	periyasamy	45	M	6/9p	6/6	MODERATE	9	13	15	>0.3	0	NO
41	usha	33	F	6/6	6/6	SEVERE	5	5	5	<0.3	4	yes
42	senthilnatha	36	M	6/12	6/6	MILD	9	13	20	>0.3	0	NO
43	sundarajan	55	M	6/60	6/36	SEVERE	8	8	8	<0.3	1	yes
44	rukumani	46	F	6/9	6/6p	MODERATE	10	12	12	>0.3	0	NO
45	rahavan	55	M	6/12	6/18	MILD	14	11	15	>0.3	0	NO
46	Poomayil	49	F	6/12p	6/18	SEVERE	10	12	14	>0.3	0	NO
47	Kaveriyamm	41	F	6/6	6/18	MODERATE	9	6	9	>0.3	1	yes
48	tamilan	25	M	6/6	6/6	MODERATE	9	15	15	>0.3	0	NO
49	mohana sur	53	M	6/24	6/18	MILD	16	14	25	>0.3	0	NO
50	Mala	47	F	6/9p	6/12	MODERATE	9	15	20	>0.3	0	NO

51	mohini	50	F	6/9	6/18	MODERATE	10	12	16	>0.3	0	NO
52	rajamani	34	F	6/12	6/6	MODERATE	8	7	10	<0.3	1	yes
53	mariyamma	42	F	6/6p	6/6	MILD	11	12	15	>0.3	0	NO
54	selvi	46	F	6/18	6/9	MODERATE	7	8	7	<0.3	1	yes
55	muniyandi	60	M	6/24	6/36p	MODERATE	7	6	8	<0.3	2	yes
56	murugeshw	42	F	6/6p	6/9	MILD	15	12	26	>0.3	0	NO
57	vijaya	35	F	6/9	6/18	SEVERE	3	5	4	<0.3	4	yes
58	raman	45	M	6/12p	6/9	MODERATE	13	12	12	>0.3	0	NO
59	selvalakshm	31	F	6/6	6/6	MODERATE	8	5	8	<0.3	2	yes
60	perumal	36	M	6/9	6/18	SEVERE	14	17	25	>0.3	0	NO
61	chellammal	52	F	6/60	6/24p	SEVERE	6	7	9	<0.3	1	yes
62	Kalaiselvi	50	F	6/18	6/24	MODERATE	8	8	10	<0.3	2	yes
63	gurusamy	55	M	6/9p	6/36	SEVERE	7	11	8	<0.3	2	yes
64	ramayee	32	F	6/18	6/9	MILD	14	18	25	>0.3	0	NO
65	karuppayee	42	F	6/9	6/18	SEVERE	8	7	12	>0.3	3	yes
66	muniyandi	52	M	6/18	6/12	MILD	12	12	16	>0.3	0	NO
67	rengaiah	58	M	4/60	6/60	MILD	13	14	25	>0.3	0	NO
68	Saraswathi	25	F	6/6	6/6	MILD	16	15	25	>0.3	0	NO
69	muthu	50	M	6/24	6/18	MILD	13	13	20	>0.3	0	NO
70	sobbammal	34	F	6/9	6/6	MILD	6	9	9	<0.3	2	yes
71	rahima beev	42	F	6/18	6/9	MODERATE	11	12	20	>0.3	0	NO
72	Packiya	46	F	6/36	6/36	SEVERE	9	9	10	<0.3	1	yes
73	muniraj	59	M	6/24	6/18	SEVERE	15	13	15	>0.3	0	NO
74	seetha	31	F	6/6	6/6	MODERATE	10	7	6	<0.3	1	yes
75	Pushpamma	40	F	6/12p	6/18	SEVERE	11	9	8	<0.3	3	yes
76	sundar	45	M	6/6p	6/6	MILD	12	13	15	>0.3	0	NO
77	Sumathy	30	F	6/6	6/9	SEVERE	11	6	9	<0.3	2	yes
78	ramar	25	M	6/6	6/6	MILD	12	16	25	>0.3	0	NO
79	kannan	53	M	6/60p	6/36	SEVERE	4	4	3	<0.3	4	yes
80	Pandiyamm	36	F	6/9	6/6	MILD	14	12	15	>0.3	0	NO
81	senthamara	55	M	5/60	6/60p	SEVERE	9	8	8	<0.3	1	yes
82	Karthikayini	28	F	6/18	6/9	MODERATE	10	9	11	<0.3	3	yes
83	Subbulakshr	42	F	6/12	6/18p	MODERATE	11	8	6	<0.3	3	yes
84	kalaiselvan	24	M	6/6	6/9	SEVERE	12	15	12	>0.3	0	NO
85	moorthi	27	M	6/6	6/6	MILD	12	14	24	>0.3	0	NO
86	Murugayam	31	F	6/9	6/6	MILD	16	15	20	>0.3	0	NO
87	Meenakshi	51	F	6/18	6/24p	SEVERE	4	1	1	<0.3	5	yes
88	sekar	34	M	6/6	6/6p	MILD	13	14	20	>0.3	0	NO
89	vennila	32	F	6/6p	6/9	MILD	15	12	17	>0.3	0	NO
90	Thangapanc	48	F	6/18p	6/18	MODERATE	11	4	6	<0.3	3	yes
91	veeran	58	M	6/36	6/60	SEVERE	6	5	8	<0.3	3	yes
92	Saroja	30	F	6/6	6/6	SEVERE	14	12	20	>0.3	0	NO
93	rajan	30	M	6/6p	6/6	MILD	15	15	23	>0.3	0	NO
94	mohan	36	M	6/9	6/6	MILD	14	12	20	>0.3	0	NO
95	prakash	38	M	6/18	6/12p	MILD	16	14	15	>0.3	0	NO
96	Vasanth	46	F	6/18p	6/24	MODERATE	12	3	7	<0.3	3	yes
97	velavan	55	M	6/60	6/24	MODERATE	6	11	9	>0.3	3	yes
98	Uma shanti	26	F	6/6	6/9	MILD	14	12	14	>0.3	0	NO
99	Jayalatha	43	F	6/18	6/18	SEVERE	9	7	10	<0.3	3	yes
100	Mariselvam	30	M	6/9	6/6p	SEVERE	13	16	15	>0.3	0	NO

KEY TO MASTER CHART

M-MALE

F-FEMALE

UCVA-UNCORRECTED VISUAL ACUITY

RE-RIGHT EYE

LE-LEFT EYE

mm-MILLIMETER

secs-SECONDS

mt-MINUTE

TBUT-TEAR FILM BREAKUP TIME

TFMH-TEAR FILM MENISCAL HEIGHT

DED-DRY EYE DISEASE

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University,
Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.P.Menaka
Course	:	PG in MS., Ophthalmology
Period of Study	:	2016-2019
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	An observational study to determine the prevalence of the dry eye disease in newly diagnosed depressive disorder patients
Ethical Committee as on	:	16.05.2018

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary

Chairman
Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc
CHAIRMAN
IEC - Madurai Medical College
Madurai

Dean / Co-Chairman
Madurai Medical College
Madurai-20

12 JUN

Fw: [Urkund] 5% similarity - menakaanandhakumar@yahoo.in

1 message

Menaka Anandhakumar <menakaanandhakumar@yahoo.in> 12 October 2018 at 12:54
To: "jeevanetcafe2010@gmail.com" <jeevanetcafe2010@gmail.com>

----- Forwarded message -----
From: "report@analysis.urkund.com" <report@analysis.urkund.com>
To: "menakaanandhakumar@yahoo.in" <menakaanandhakumar@yahoo.in>
Sent: Thursday, 11 October, 2018, 12:08:19 PM IST
Subject: [Urkund] 5% similarity - menakaanandhakumar@yahoo.in

Document sent by: menakaanandhakumar@yahoo.in
Document received: 10/11/2018 8:37:00 AM
Report generated 10/11/2018 8:38:16 AM by Urkund's system for automatic control.

Student message:

Document : MENAKA DISSERTATION.doc [D42404537]

IMPORTANT! The analysis contains 1 warning(s).

About 5% of this document consists of text similar to text found in 87 sources. The largest marking is 62 words long and is 86% similar to its primary source.

PLEASE NOTE that the above figures do not automatically mean that there is plagiarism in the document. There may be good reasons as to why parts of a text also appear in other sources. For a reasonable suspicion of academic dishonesty to present itself, the analysis, possibly found sources and the original document need to be examined closely.

Click here to open the analysis:
https://secure.urkund.com/view/41441054-940027-732937

Click here to download the document:
https://secure.urkund.com/archive/download/42404537-919359-413626

CERTIFICATE

This is to certify that this dissertation titled "**AN OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF THE DRY EYE DISEASE IN NEWLY DIAGNOSED DEPRESSIVE DISORDER PATIENTS** "of the candidate **Dr.P.MENAKA** with registration number **221613103 f**or the award of **M.S degree in the branch of Ophthalmology**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **5percentage** of plagiarism in the dissertation.

Guide and supervisor sign and seal